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JOHN H. MUSSER, JR.

AN APPRECIATION.

DR. JOHN H. MUSSER's removal to New Orleans to accept the chair of medicine at Tulane University has necessitated his resignation as Editor of this Journal, thus terminating a ten-year connection. Appointed Assistant Editor in 1914, under Dr. G. M. Piersol, Dr. Musser continued in this position until on Dr. Piersol's resignation in 1922 he became the Editor—the ninth to hold this position in 105 years. The previous editors were Nathaniel Chapman, 1820; Isaac Hays, 1833; I. Minis Hays, 1879; E. P. Davis, 1891; Alfred Stengel, 1899; F. R. Packard, 1901; A. O. J. Kelly, 1906; G. M. Piersol, 1911.

In spite of his numerous institutional duties and the ever increasing demands of a rapidly growing practice, he always found time to do more of the editorial work than his associate editor thought proper. The eight-hour working day, however, was literally almost doubled in the process, and the time necessary for first-class scientific work became more and more difficult to obtain. At Tulane, on the other hand, as full-time head of an important department of a progressive school, Dr. Musser should have ample opportunity to render a splendid service to medical education, as well as to satisfy his own intellectual requirements. Much as his Philadelphia friends will miss him, they must recognize that his recent decision was a wise one. During Dr. Musser's editorship, the policy of the Journal continued with very little change. His constant attention to possible improvement in the form of its contents and the quality of the English used in its articles was not without results—a trend in a direction for which there is still much room for improvement in American medical literature.

In the first number of the Journal (*The Philadelphia Journal of the Medical and Physical Sciences*, 1820, **1**, 1), its editor, Nathaniel Chapman, thought it necessary to quote from the Edinburgh Review: "What does the world yet owe to American physicians and surgeons?" as a reason for his venture. Though an unfair criticism even then, certainly it is not one that would even be suggested today. And yet the present editors feel now as much as then the necessity, in the words of Chapman's prospectus, "to evolve and stimulate the genius of the country to invigorated efforts . . . We look to the profession at large for countenance and support of a scheme that deeply concerns the whole, and which we are sensible can only succeed by general appreciation and cordial coöperation." If this can be secured, we have high hopes that we can succeed in maintaining it, even in the face of the rapidly changing conditions of medical journalism in this country, as Sir William Osler said, "one of the few great journals of the world."

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

MARCH, 1925

ORIGINAL ARTICLES.

REFLECTIONS ON THE INTERPRETATION OF SYSTOLIC CARDIAC MURMURS.*

By William S. Thayer, M.D., F.R.C.P.I. (Hon.),
BALTIMORE, MD.

The art of prognosis with which the insurance examiner is especially concerned, is one of the most important branches of medicine.

But unless prognosis springs from solid diagnostic roots the tree is unstable.

The art of prognosis may, under some conditions, depend largely on the consideration of figures and statistics based on scientific analyses of accumulated observations.

The art of diagnosis must always depend, in large part, on the observation, the care, the skill, the intelligence and the reasoning power of the individual examiner.

The ability and the reliability of the individual examiner, on the results of whose reports conclusions are to be reached, constitute the corner stone of the prognostic art.

As one who has, for many years, been especially interested in diagnostic problems, and has taught physical diagnosis off and on for thirty-four years, it is naturally from the diagnostic standpoint and from my own experience rather than from a review of the literature that I shall approach this subject.

In what is rapidly becoming a fairly long experience, I am rather impressed with the frequency of what seems to me an unfortunate attitude of student and physician in approaching certain diagnostic

* Remarks made before the Medical Section of the American Life Convention at Atlantic City, June 4, 1924.

problems. We hear, let us say, a modification of a heart sound. We make note of a "systolic murmur at the apex;" and forthwith the mind jumps to a consideration of cardiac murmurs in the abstract before we have given sufficient thought to the vital question, which only we can decide intelligently, namely, what may be the cause of this particular sound in the concrete case.

If we are incapable of exercising our reason on the basis of simple anatomical, physical and physiological considerations, not all the statistics in the world can make us intelligent or competent diagnosticians. Too many accept the statements of others; too few reflect for themselves on the simple physical conditions on which a cardiac murmur may depend.

I am, for instance, impressed by a statement that appears on page 10 of your excellent little pamphlet *à propos* of systolic murmurs in the second right space: ". . . in older applicants (they) may indicate arterio-sclerotic roughening at the aortic orifice."

It is never safe to make positive assertions in medicine. I am, however, not aware that evidence has ever been presented of the origin of any of these common murmurs, other than those dependent upon a true stenosis, from "roughening" at an orifice. An adequate explanation of the origin of such murmurs is not difficult to find. But the true explanation, I venture to fancy, has nothing to do with a "roughening" of the orifice, which, as a matter of fact, excepting in stenoses, is not found anatomically.

Let us for a moment reflect on some of the conditions associated with the origin of systolic murmurs.

Reduced to its simplest terms the "constatation," as the French say—an admirable word meaning observation with appreciation for which I know no equivalent in English—the constatation of a systolic murmur at some point in the circulatory apparatus means the presence of audible vibrations of the vessel wall resulting from the passage of blood from a narrower suddenly into a wider cavity, or through a constricted area in the course of the tube. Whatever the physical possibilities as to the origin of vibrations in fluid currents, it is doubtful whether murmurs that are clinically appreciable ever arise in another way.

The manner of origin of a murmur may be illustrated simply and satisfactorily by pinching a rubber tube through which water is flowing. Beyond the point of constriction there arise a palpable thrill and an audible murmur, appreciable only when the current becomes of sufficient rapidity. This murmur is transmitted in the course of the current; it is but feebly heard back of the point of its origin. Other things being equal, murmurs arise more readily in thin fluids of low viscidity and specific gravity, flowing at a high rate of velocity.

When one considers the structure of the heart there are certain points at which one might expect murmurs to arise in the ordinary course of events. Such points are notably the *aortic* and *pulmonic*

rings. These rings, fibrous structures, more or less constant in their circumference, and incapable of notable dilatation during the cardiac movements, connect the proximal ventricles which may vary considerably in their strength and in the quantity of blood that they eject, with the distal vessels which are of great elasticity and capable of wide dilatation.

Here, indeed, are most of the specifications one could demand for the construction of a model to illustrate the origin of vascular murmurs—a ventricle which throws more or less blood with more or less force through a fixed ring into a dilating vessel beyond. It is doubtful whether man could construct such a model which would fail to produce a systolic murmur when put into operation.

Why, then, do we not always find systolic murmurs at aortic or pulmonary orifices? This is a question that we cannot answer save by the recognition that nature has so admirably adjusted ventricle, ring and vessel that in normal function, they act as if parts of one elastic tube of constant size.

Palpable and audible vibrations arise, of course, less readily in a viscid medium like blood than in water. But, as a matter of fact, it is just at these points—the aortic and pulmonic orifices—that systolic murmurs are commonest in the normal human being, and of the least significance.

Aortic Orifice. Experimentally[1] in living dogs, murmurs may be caused at the aortic orifice:

(1) By producing an actual stenosis.
(2) By bleeding followed by infusion of salt solution, through which the blood is rendered more fluid.
(3) When conditions are produced in which the excursion of the pulse is greater; that is, in which there is a greater dilatation of the aorta with each systole—as, for instance, in aortic insufficiency.

In the human being such murmurs at the aortic orifice are observed:

(1) With actual aortic stenoses.
(2) In dilated and hypertrophied hearts, notably in aortic insufficiency where, with a ring of relatively normal size, a ventricle larger and stronger and with greater capacity, is throwing blood into an aorta capable of wide dilatation.
(3) With permanent dilatations of the ascending aorta above the ring which are so common either with syphilis or in old age.
(4) Without obvious cardiac abnormalities, in anæmia—diminished viscosity of the blood—and not infrequently in young neurotic individuals with throbbing vessels—the sort of people in whom loud murmurs are heard in the pulmonary area.

[1] Thayer and MacCallum: Am. Jour. Med. Sci., 1907, **133**, 249.

But these are precisely the conditions in which murmurs may be induced experimentally.

In other words, where the ventricle is dilated or hypertrophied or wherever the aorta beyond the ring is relaxed or dilated or wherever the ring itself is narrowed, one may and often does observe a systolic murmur at the aortic orifice.

True stenoses may be recognized by a variety of characteristic phenomena.

Aortic insufficiency, in which systolic murmurs are so very common, is always pathological and easily recognized.

Soft systolic murmurs in the young or in the anæmic, if unassociated with other signs, we have learned fairly well to disregard.

Similar aortic murmurs in men of middle life or past middle life are those which attract our suspicion and demand our attention.

In most cases, with or without evidences of cardiac hypertrophy, such murmurs, in the absence of actual stenoses, will be found to be associated with moderate dilatation of the arch. Dilatation of the arch, often difficult to recognize before the days of roentgenology, is, as is well known, especially common with syphilitic changes which may lead to true aneurysm formation, but it is also exceedingly common with the arterio-sclerosis of age.

These are the murmurs to which I referred a minute ago which are so often ascribed to "roughnesses."

Anyone, however, who is familiar with the pathological anatomy of the aorta must realize that syphilis rarely if ever results in roughnesses which could easily be imagined to set the blood of the entire aorta into audible vibrations; even the extensive calcified plaques of a senile arterio-sclerosis do not, as a rule, give rise to murmurs elsewhere along the course of the vessel.

The cause of these systolic murmurs is the actual or relative dilatation of the ascending aorta above a normally rigid ring. If there be not a true stenosis there is always a relative stenosis depending upon aortic dilatation; this, I venture to assert, is the one adequate explanation of these murmurs.

Murmurs in the Pulmonary Area. The region of the pulmonary artery and conus arteriosus—the second and third left spaces close to the sternum—is the commonest seat of systolic murmurs.

Experimentally, murmurs at the *pulmonary orifice* may be produced in the same way as at the aortic ring:

(1) By artificial stenosis which may be induced by the very slight pressure of the stethoscope on the thin-walled conus.
(2) By bleeding and infusion of salt solution.
(3) When, in the course of the experiment, conditions arise which result in an abrupt cardiac contraction and high pulse pressure in the pulmonary artery.

Clinically, the frequency of murmurs in this area is familiar. They occur:

(1) With actual stenoses.
(2) Normally in young individuals, and notably in the neurotic, exaggerated or induced by forced expiration and often disappearing on full inspiration.
(3) In anæmia.

The pulmonary artery and the conus lie close to the chest wall. In the young with elastic lungs and a large cardiac incisure, the conus may impinge directly upon the chest wall. This impinging during systole against the chest wall should reproduce exactly the conditions which exist experimentally when one presses a stethoscope against the conus.

With a deep inspiration, however, a soft cushion of lung is interposed between ventricle and chest; under these circumstances the murmur disappears.

Auriculo-ventricular Orifices. If it be true that with normal cardiac function the ventricle, the arterial orifice—constriction through it may appear—and the vessel beyond so comport themselves as to represent a single tube, the same is true of auricle, atrio-ventricular orifice and ventricle in diastole.

The tricuspid and mitral rings in normal function behave not as straits, but as parts of a common auriculo-ventricular canal. Only with actual stenoses of these orifices do audible or palpable vibrations arise when the blood is flowing in its normal course.

Apical Systolic Murmurs. But, as is familiar, systolic murmurs may arise at the auriculo-ventricular orifices.

Experimentally, apical systolic murmurs may be produced in the dog by incision or laceration of the mitral valve. This, as one might expect, results in:

(1) Palpable and audible vibrations arising at the opening through which the regurgitant current passes backward into the auricle; the opening is a point of constriction in the course of the regurgitant blood. The thrill and murmur at this point are usually of great intensity. But the auricular wall adjacent to the mitral valves cannot be reached even in the widely open dog's chest, save by awkward manœuvres. As the heart lies in position one cannot reach the auricle; one can place the stethoscope directly over the left ventricle only at the apex of the heart. But this point, lying proximally to the seat of origin of the vibrations, is, physically, a relatively unfavorable spot for the transmission of the sound. In experimental mitral insufficiency the thrill, so easily palpable on the auricular side of the valves, is lost at the apex where the murmur, instead of being harsh and rasping, becomes soft and blowing, like the systolic murmur of mitral insufficiency as heard in the human being.

(2) Like murmurs arise without valvular damage on the development of dilatations of the mitral ring which may be brought about by overdistending the heart or as a result of failure of the muscles toward the end of the experiment.

Experimentally, then, in the dog, systolic murmurs heard best in the region of the apex and similar to those heard in mitral insufficiency in the human being, may be produced by damage to the mitral valve or by dilatation of the auriculo-ventricular orifice.

Clinically, in the human being, a systolic murmur heard in the region of the apex is a common phenomenon.

Such murmurs are observed:

(1) In disease of the valves resulting in insufficiency.

(2) In muscular weakness resulting in dilatation of the mitral ring, which is observed under a variety of conditions.

(3) Normally, as so-called functional murmurs, the commonest varieties of which are

(*a*) Apical systolic murmurs in normal young individuals heard in the recumbent and left lateral posture.

(*b*) Cardio-respiratory systolic murmurs.

Apical systolic murmurs are not generally of very great intensity for the obvious reason that the points at which we are able to approach the heart with our stethoscopes are situated proximally to the point of origin of the murmur. They are commonly heard in axilla and back because, even though considerable lung be interposed between heart and chest wall, the root of the left ventricle and the left auricle over which the murmur is of greatest intensity, lie posteriorly.

It is well to remember in connection with indirect mitral murmurs, as with direct aortic murmurs, that the cause of the murmur is the passage of blood through a narrow orifice into a wider chamber, and not, as a rule, the result of interference with the current by vegetations or roughnesses at the orifice itself, save in the case of large calcified masses. It is not likely that vegetations in themselves play any essential part in producing audible vibrations save, perhaps, the large thrombotic vegetations of a bacterial endocarditis.

The assumption that the systolic murmur of mitral insufficiency is usually due to roughnesses and vegetations on the valves, even in acute rheumatic endocarditis, is very common. One has, however, but to reflect on the character of the lesions of acute rheumatic endocarditis to realize that the tiny verrucosities along the line of meeting of the valves would be quite incapable, of themselves, of producing sonorous vibrations. The early murmurs arising at the mitral orifice in acute rheumatic heart disease are not due to the endocarditis but to the relaxation of the mitral ring due to myocardial change. It is only with the subsequent chronic thick-

enings and curlings of the valve curtains and shortening of the chordæ tendineæ, that recognizable insufficiencies and stenoses occur. This is why all cases of acute rheumatic fever should be kept under observation for weeks or months after recovery from the acute symptoms. In many such cases the appearance of chronic valvular disease gives evidence of a previously unrecognized acute change;[2] in others the disappearance of the murmur proves its myocardial origin.

But how about those obvious insufficiencies with grave cardiac failure that may occur relatively early in an attack of acute rheumatism? Are we wrong in assuming that these indicate the existence of an endocarditis?

Yes and no.

We are *wrong* in the sense that an acute rheumatic endocarditis could not of itself produce such signs and, as a matter of fact, has nothing to do with them. *But acute rheumatic heart disease is, in almost all cases a pancarditis,* and the early cardiac dilatation which results in the systolic murmur is dependent upon the acute myocarditis.

We are *right* in assuming that these signs are suggestive of an acute endocarditis because, in the great majority of cases, endocarditis accompanies the myocardial and pericardial changes.

1. *That a given apical systolic murmur may depend upon actual valvular disease* is suggested by:
   - (*a*) The history of previous conditions commonly associated with endocarditis — rheumatism, chorea, repeated tonsillitis.
   - (*b*) Evidences of an associated bacterial endocarditis.
   - (*c*) The coincidence of signs of mitral stenosis.
   - (*d*) The presence of a murmur of a specially harsh and rasping character.

2. *That such murmurs depend upon dilatation of the mitral ring* may be suggested by:
   - (*a*) The absence of a history pointing to preëxisting valvular disease.
   - (*b*) Their development in the course of progressive hypertrophy and dilatation from hypertension or syphilitic aortic insufficiency.
   - (*c*) Their appearance in the course of acute infectious fevers not commonly associated with endocarditis or in grave anæmias with great muscular weakness.
   - (*d*) Acute heart failure occurring in the early stages of rheumatic heart disease.

3. *That the murmurs are functional* and of no pathological significance may be suspected:

[2] Thayer: Jour. Am. Med. Assn., 1906, 47, 1352.

(*a*) *In young people under thirty years of age, especially in women but often in boys when the patient is examined in the recumbent posture and when the murmur is accompanied by a louder murmur in the pulmonary area.* Under these circumstances systolic apical murmurs are very common. The heart sounds are generally of a normal character but the first sound at the apex is followed by a fairly distinct whiff which may or may not be transmitted into the axilla. The murmur is usually increased when the patient lies in the left lateral posture. These murmurs are generally heard all over the heart and loudest in the pulmonary area; but *sometimes* they are loudest at the apex, and sometimes they are not heard at the base. In the erect posture, the murmur disappears at the apex and diminishes in intensity if it does not disappear at the base on full inspiration. Sometimes it disappears at the apex on full inspiration suggesting that it is a transmission of the basic sound.

Such murmurs are extremely common and of no pathological significance.

During my studies of the third heart sound some years ago, among 218 apparently healthy individuals in the first four decades of life, 74 or over one-third showed systolic murmurs at the apex in the recumbent posture.

FREQUENCY OF SYSTOLIC MURMURS AT THE APEX OF THE HEART IN OTHERWISE NORMAL INDIVIDUALS IN THE RECUMBENT POSTURE.

Decades	1*	2	3	4
Cases	39	98	55	26
Murmurs present	22	35	12	5
Percentages	56.4	35.7	21.8	19.2

Among 30 healthy school boys in the second decade of life, 18 (60 per cent), showed systolic cardiac murmurs. In all, the murmur was heard in the pulmonic area; in 13 (43.3 per cent), it was audible at the apex as well as in the recumbent or left lateral posture. In the erect posture the heart sounds were clear at the apex.

I am inclined to think that in most instances, the systolic murmur heard at the apex in the recumbent and left lateral posture is but a transmission of the basic sound although it has, in my mind, always been a question whether posture may not, sometimes, cause a true functional mitral insufficiency.

(*b*) *In the case of cardio-respiratory murmurs,* with the abrupt emptying of the ventricles in systole the place

* None under three years.

occupied by the full ventricle is compensated for by a slight collapse of the overlying chest and an accentuated rush of air into the overlying lung. This brings it about that, with each systole, there is, often, a rhythmical accentuation of the inspiratory murmur and sometimes even a slight sound during expiration. This sound may be extraordinarily like the murmurs depending on an actual mitral valvular insufficiency. That it should be similar in character has been explained by studies in Mueller's[3] Clinic which show that the physical characteristics (the dominating tones of the ordinary inspiratory murmurs) are very close to those of the common systolic murmurs of mitral insufficiency.

Cardio-respiratory murmurs are sometimes heard with greatest intensity toward the base, more often, in my experience, toward the apex of the heart. They are always accentuated during inspiration, and usually disappear at some stage of respiration, generally when a full breath is held. They are always recognizable to the careful student, but if one does not pay careful attention, they may be very misleading. This is especially true since it is not generally appreciated *that these murmurs may be heard with greatest intensity in the back over the left lung*, notably in young individuals with throbbing hearts. I have seen more than one false diagnosis of organic heart disease made in such cases where a little careful attention would have made the nature of the murmur perfectly clear.

Systolic murmurs arising at the tricuspid orifice I shall not discuss.

Summary. I have tried especially to emphasize several simple points:

1. That it is not the frequency of soft systolic murmurs at aortic and pulmonary orifices that is remarkable. What is remarkable is that they are not always present.*

2. The presence of such murmurs depends upon the relative stenosis represented by the more or less rigid aortic or pulmonary ring and the dilatability or dilatation of the vessel beyond. The frequency of such murmurs at the aortic orifice in later life is, in the majority of instances, dependent upon a greater or less dilatation of the arch, not upon roughnesses at the aortic ring.

3. The frequency of functional systolic apical murmurs in the young when in the recumbent posture.

4. The importance of recognizing cardio-respiratory murmurs and the realization that they are often heard with considerable intensity in the back.

[3] Lancet, London, 1913, **1**, 674.

* This remark is not original. It has been made, I think, by Broadbent.

STUDIES IN HUMAN CONSTITUTION: FACIAL FORM AND DISEASE CORRELATION.

By George Draper, M.D., Halbert L. Dunn, M.D.,
and
David Seegal, M.D.

(From the Department of Medicine of the Columbia University, College of Physicians and Surgeons and the Presbyterian Hospital.)

There is no doubt in any one's mind that, for him who has learned to read it, the face of Man is an open book. Indeed clinicians have placed such great value upon the facial expression of sick people that in some instances, as for example the "Hippocratic facies," a diagnosis is based upon it. In Dorland's medical dictionary there are thirty-two different disease facies described. But like much of the information which free observation brings to the physician, it is often difficult for him to define just what it is that he has seen. Strangely enough too, the most carefully trained doctors, in respect to correlations between facial aspect and disease, have used essentially the arts of the physiognomists and phrenologists. These supposedly fanciful observers, however, who have sought to make correlations between psychic pattern and facial form, have at least attempted to base their anatomical data upon definite measurement. John Hunter,[1] Blumenbach,[2] Cuvier[3] and Petrus Camper[4] all studied the comparative relationships of face and head size. The work of these observers was stimulated partly through interest in the different races of mankind and partly by a desire to correlate with facial form the psychological, emotional and temperamental differences between races and individuals. Darwin[5] made many observations upon facial expression. Still later Laycock[6] wrote extensively on "Physiognomical Diagnosis."

In connection with the general study of human constitution, which is in progress at the Presbyterian Hospital, our attention has been drawn to certain measurable recurring facial characteristics. In this study of constitution, as was pointed out in a previous paper,[7] all patients have been divided into groups according to the disease from which they suffer. In the present report interdisease group comparisons have been made between the anatomical facial differences of 5 disease types, namely, people having gall bladder disease, gastric and duodenal ulcer, nephritis hypertension, pernicious anemia or tuberculosis.

The material upon which the study is based consists of 280 cases: 161 males and 119 females. Seventeen of the 161 male patients belong to the gall bladder group, 21 to the pernicious anemia, 18 to the nephritis hypertension, 30 to the gastric and duodenal ulcer

and 75 to the tuberculosis. Thirty-three of the 119 females were gall bladder patients, 23 pernicious anemia, 20 nephritis hypertension, 15 gastric and duodenal ulcer and 28 tuberculosis.

In analyzing the variation between human faces it is necessary first to define what constitutes the face (Fig. 1). The usual conception of the face is a perpendicular oval bounded superiorly by the hair line. Anthropometrically, however, the face is limited superiorly by a horizontal line drawn through the nasion. In this more restricted sense, the face is a more or less squat horizontal truncated oval; the facial diameter being always of greater length than the facial height.

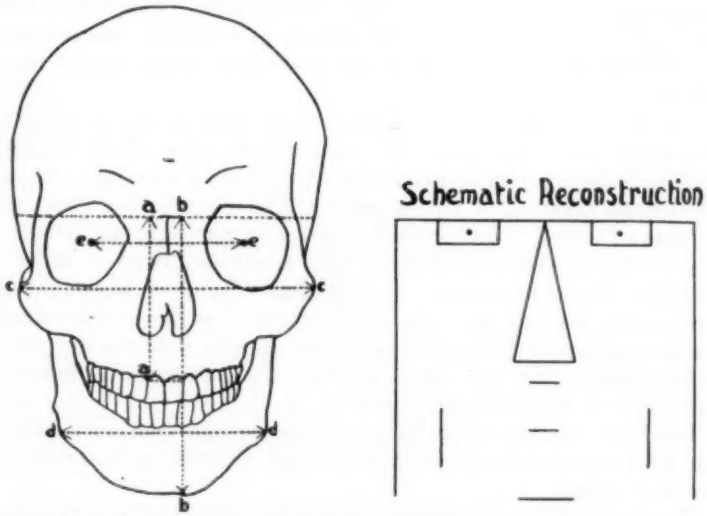


FIG. 1.—Facial measurements. aa, nasion prosthion (upper facial height); bb, facial height; cc, facial diameter; dd, gonial diameter; ee, interpupillary space.

The facial measurements which have been used are 10 in number: (1) Nasion prosthion (aa, Fig. 1), from the nasion to the maxillary alveolar point; (2) the facial height (bb, Fig. 1), from the nasion to the menton (mental tubercle); (3) facial diameter (cc, Fig. 1), the widest interval between the zygomatic arches; (4) bigonial diameter (dd, Fig. 1) or distance between the angles of the mandible; (5) interpupillary space (ee, Fig. 1) taken to the center point of each pupil; (6) infradental menton, distance from the mandibular alveolar point to the mental tubercle; (7) nasal height, from the nasion to the lower border of the nose, where it meets the lip; (8) nasal breadth, distance between the outer surface of the alæ nasæ; (9) palpebral length or length of the eye slit and (10) palpebral breadth, the greatest distance between the upper and lower lids with the eye fixed on a distant object.

The schematic reconstruction of these measurements, as shown in Fig. 1, illustrates the inadequacy of anthropometrical determinations for reproducing what is seen by the human eye.

Obviously the good clinician sees much more in the face of his patient than can be measured by instruments. That which he observes is a summation of three distinct elements:

The element which the eye catches first and most readily is that produced by the distribution of the soft parts and by the muscles of expression. The scope of this paper however, cannot include a discussion of expression, a subject which has been dealt with at great length by scientists, philosophers, and artists. But it is important to remember that almost every degree of form and expression may clothe the same bony framework. Emotional influences, physical conditions, malnutrition or endocrine disturbances may change the expression of the same individual beyond recognition.

The second element is the strong impression produced solely by differences in actual size. To demonstrate this effect we have compared the average facial measurements of 21 pernicious anemia males with those of 9 acromegalics. The pernicious anemia and acromegalic faces were reconstructed schematically as shown in Fig. 1 and the angle of the jaw was arbitrarily fixed in order to complete the facial outline. It is evident (Fig. 2) at once that the acromegalic features are very much larger than those of pernicious anemia people. When the pernicious anemia features are raised proportionately to the same scale as the acromegalic, however, they prove to be practically identical.

The third element is the effect of relative size or in other words true proportional differences. This third element will now be discussed in detail.

The study of relative differences has been made by intercomparison of the bony measurements and the interpupillary space. These have been related to one another as indices.

Three indices have been used and are shown in Fig. 1:

The first or facial index is formed by dividing the facial height by the facial diameter and multiplying by 100. It expresses facial height in per cent of facial diameter. It is an index of the relative breadth or length of the face as a whole. Consequently a low index means a wide, short face.

The second or upper facial index is formed by dividing the nasion prosthion length by the facial diameter and multiplying by 100. It expresses the relative width of the upper facial zone, or that region which lies between the nasion and the mandible. A diminishing index here signifies a wide, short upper facial zone.

The third index expresses the relative proportions of the eye-nose zone. It is formed by dividing the interpupillary space by the nasion prosthion and multiplying by 100. It is important to observe that

unlike the two preceding indices this one is formed by dividing a breadth by a vertical measurement. As the index becomes smaller the nasion prosthion grows larger and, therefore, a small index signifies a narrow eye-nose zone.

The relative differences between disease groups are proven by indices and by arithmetic averages. The graphs, Figs. 3 and 4,

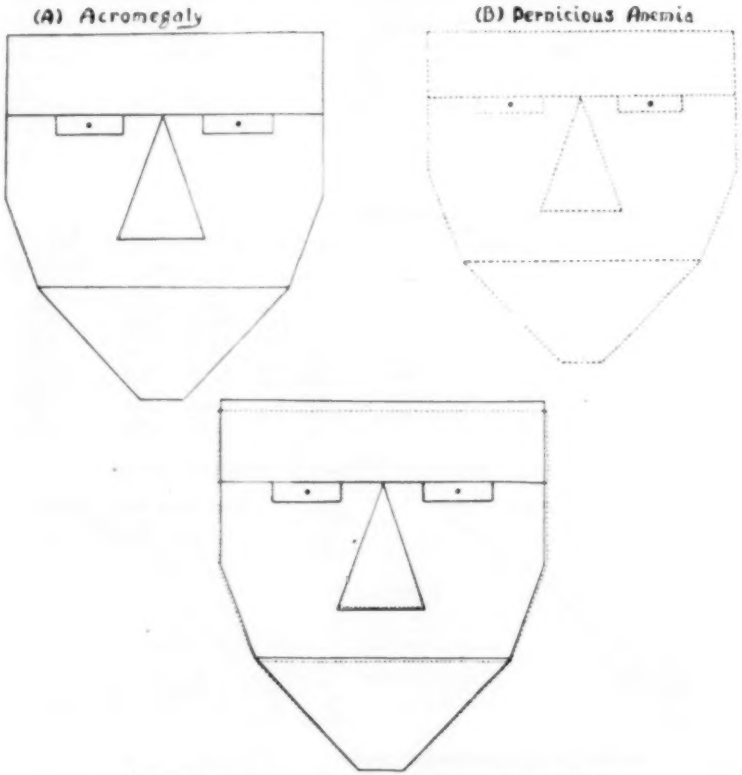
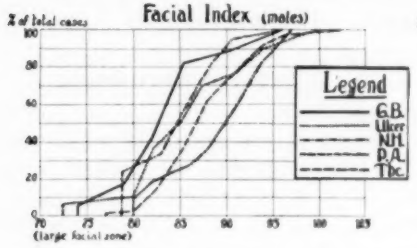


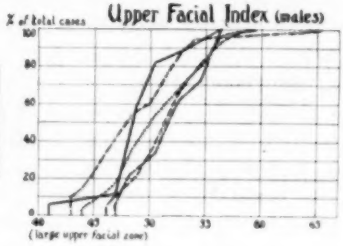
FIG. 2.—Actual and relative comparison of face size and shape. *A* and *B*, actual size: *C*, relative size.

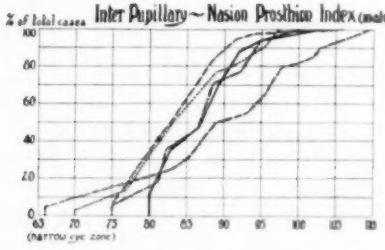
are accumulative percentage frequency curves, the ordinates of which represent the per cent of total number of cases and the abscissæ the value of the respective index. These curves are of primary value in showing the distribution of individual cases. The table is based on arithmetic averages of the data. Three measurements are recorded in per cent of facial height and the interpupillary space is also given in per cent of the facial width.

The anatomical facial differences between the 5 disease groups (Figs. 3 and 4) may be summarized as follows:

In all disease groups the face of the male is consistently more narrow in proportion to its height than is that of the female.

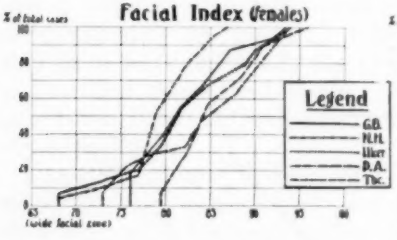


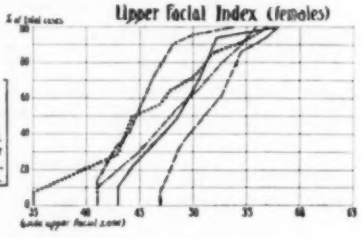


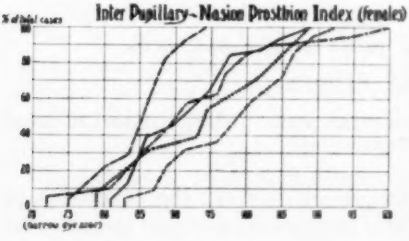


Dis-ease	Width Measurements in Percent of Facial Height: Facial Diam.	Bi-Gonial Diam.	Inter-Pupillary Space	Facial Diameter: Inter-Pupillary Space
PA.	117	90.3	53.0	45.3
G.B.	118	87.3	51.3	43.4
Ulcer	115	86.8	50.2	43.8
N.H.	111	84.5	51.2	46.0
Tbc.	113	84.7	49.6	43.9

FIG. 3.—Facial differences in males in five disease groups.







Dis-ease	Width Measurements in Percent of Facial Height: Facial Diameter	Bi-Gonial Diameter	Inter-Pupillary Space	Facial Diameter: Inter-Pupillary Space
PA.	12.4	92.1	56.9	45.9
GB	12.0	90.4	54.4	45.3
Ulcer	12.0	89.2	54.9	45.7
N.H.	12.0	88.2	55.5	46.3
Tbc.	11.3	87.2	51.7	44.8

FIG. 4.—Facial differences in females in five disease groups.

Gall bladder and pernicious anemia people have wide faces and wide upper faces. The female faces of the pernicious anemia individuals are considerably wider than those of the gall bladder people.

Pernicious anemia people have wider lower faces than do the gall-bladder as shown by the relatively large bigonial diameter for both male and female. They also have much wider eye zones than the gall bladder people as demonstrated by the interpupillary-nasion prosthion index. Nephritis hypertension people and tuberculosis

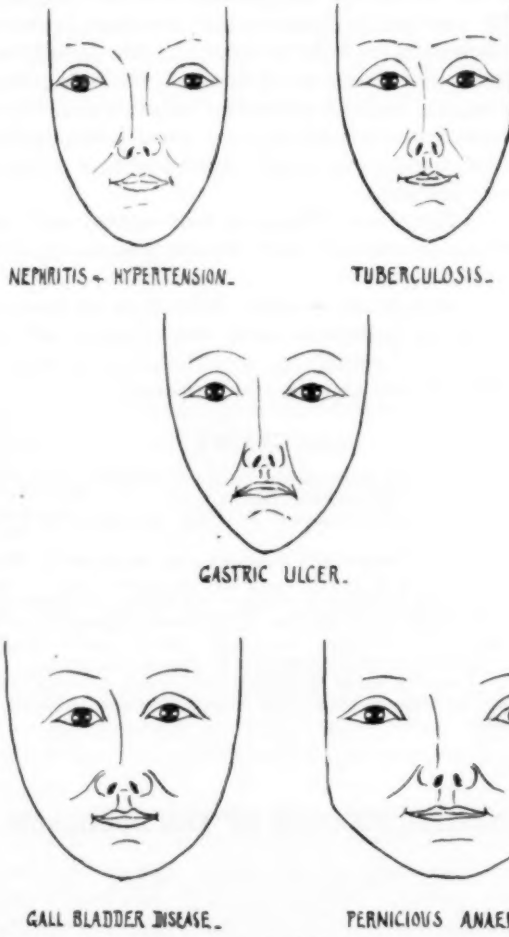


FIG. 5.—Semischematic faces, emphasizing basic proportional differences.

individuals, on the other hand, have relatively narrow faces. The nephritis hypertension group has comparatively broad eye zones in contrast with the tuberculosis type which has very narrow ones. Ulcer people are intermediate in all respects. The accumulative percentage distribution curves check with the results based on the arithmetic averages. When the interpupillary space is expressed

in per cent of the facial width, the nephritis hypertension of both sexes appear to be particularly wide-eyed because of their narrow faces. The gall bladder individuals, on the other hand, have narrow set eyes in respect to the width of their faces.

The principal differences between the faces of various disease types (Fig. 5) are shown by exaggerated sketches based on these mathematically proven variations: (1) the long, thin nephritis hypertension face with its wide set eyes; (2) the equally long, thin tuberculosis face with its narrow set eyes; (3) the wide rounded gall-bladder countenance with its relatively narrow eyes; (4) the wide pernicious anemia features with its very great interpupillary space and its wide jaw angles; and finally, the ulcer face which is intermediate in every respect.

Summary. 1. There are differences both actual and relative in the bony skeleton of the face and the eye placement of different disease races.

2. The good clinician can observe differences between the faces of his patients by analyzing separately the effect of soft parts and expression, the effect of actual size, and the effect of relative differences in the facial indices and the eye placement.

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CONGENITAL FIXATION OF THE DUODENUM.

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The frequent occurrence of adhesions or bands within the peritoneal cavity has long been recognized by pathologists and anatomists, Virchow,[1] in 1853, having published a comprehensive and instructive article on the subject. They were formerly regarded as inflammatory in origin but evidence has accumulated which shows quite conclusively that in fetal and early life, at least, they are congenital, and that most of those occurring in later life are likewise due to developmental defects.

Important observations have been recorded by Morris,[2] Robinson,[3] Opitz,[4] and others; but by far the most valuable have recently been published by Bryant[5] whose painstaking observations and analyses form a basis for the most accurate data now available. He concludes that the frequency of occurrence of peritoneal bands has been greatly underestimated, as he found them present in 91.1 per cent of his male cases, which included 18 fetuses, and in 85.5 per cent of the female cases, which included 16 fetuses.

Convincing evidence regarding the developmental origin of such bands is also found in Bryant's observation that until the age of forty there is no material increase in the frequency of peritoneal bands above the percentage of involvement found in fetuses. Furthermore, he observed that the bands which are found with the greatest frequency in adults are the ones most frequently found in fetuses. The developmental or congenital origin of these folds, or membranes, or adhesions, can, therefore no longer be doubted.

The types of bands found and their frequency in both sexes as reported by Bryant is shown in the following table:

	Male, per cent.	Female, per cent.
Gall bladder to the duodenum and the transverse colon	25.6	24.8
Gall bladder to the transverse colon	17.2	9.4
Gall bladder to the duodenum	15.5	17.9
Appendix to the peritoneum	15.0	5.9
Omentum to the ascending and the transverse colon	11.1	12.0
Ascending colon to the transverse colon	10.6	5.9
Duodenum to the peritoneum	6.7	10.3

A study of this table shows that in both sexes the bands which have their origin around the gall bladder comprise a majority of all the bands which were observed, namely, 57.3 per cent in the male cases and 59.7 per cent in the female cases. Harvey (reported by Homans) studied the frequency of bands running from the gall-bladder to the duodenum in infants and found them present in 19 per cent of his cases, a figure which compares with Bryant's very closely.

It appears evident, therefore, that the frequency of congenital bands in the abdomen has heretofore not been appreciated and my observations lead to the conclusion that their clinical significance is of greater importance than is generally realized. Several types of bands are often found in the same individual as shown by Bryant's table of frequency mentioned above, and any or all of them may play a part in producing symptoms. I shall, however, confine my remarks to the most frequent type, which also, I believe, causes the most severe and definite symptoms, namely, those which have their origin about the gall bladder and pass to the duodenum alone, or to the duodenum and the transverse colon.

The first to appreciate the clinical significance of the hepato-duodenal type of band, so far as I know, was M. L. Harris,[6] who in

1914 reported a group of 6 cases on whom he had operated upon with uniformly gratifying results, and in our clinic we have come to refer to them as "Harris' Bands." Since the publication of Harris' paper, 2 other series have been reported, 1 by Homans,[7] who in 1916 reported 17 operated cases, and in 1917 Hill[8] reported 4 operated cases. Although I recognized several cases soon after reading Harris' report, I was then inclined to regard it as a rather rare condition and relatively unimportant; but further observations have convinced me that it is frequently the cause of distressing symptoms and I believe that a considerable percentage of the illy-defined, chronic disturbances of the gastrointestinal tract which are variously diagnosed as chronic colitis, auto-intoxication, enterostasis, periduodenal adhesions, and so forth, have their origin in this kind of lesion. During the past ten years, 39 of my patients have been operated upon for this condition and their records form the basis for my report. I have also seen about 150 others in whom the diagnosis was made but who for various reasons have not been operated upon.

Of my 39 cases operated upon, 31 (80 per cent) have been females and 8 (20 per cent) males. The greatest number, 15, have been in the third decade when operated upon. The youngest was fifteen years of age, the eldest 67. The duration of symptoms varied from six months to twenty years, the average being about twelve years. In general the older the patient the longer the complaint of symptoms.

A review of the histories shows that in almost all instances digestive disturbances existed in infancy and childhood. Some were difficult babies to feed, some had eczema, several were reported to have had "cyclic vomiting" or acidosis. Some vomited when fatigued, or emotionally upset; others had "bilious attacks" and headaches; three had epilepsy and practically all always had been constipated.

So far as symptoms are concerned, the cases may be divided into two classes, (*a*) those characterized by attacks of epigastric pain, and (*b*) those which are toxic and complain of indigestion, usually not painful. It is impossible to sharply separate these classes for those in which paroxysms of pain predominate always show some evidence of intoxication and the toxic cases usually, though not always, have some epigastric pain at times.

The painful cases are less numerous than the toxic, 12 (30 per cent) having been so classified. A typical example is that of a woman, aged thirty-four years, who always had been constipated but generally well. One morning, seven years ago, she arose feeling perfectly well and went to business as usual. About two hours after a hearty luncheon she began to have pain in her epigastrium. It was not agonizing but compelled her to go home and kept her awake all night, subsiding the next morning when her bowels moved.

It was felt chiefly beneath the ribs on the right side of the epigastrium and did not radiate. It varied in intensity from time to time but there was no cessation at any time. She belched gas but was not nauseated and did not vomit. During the next four years she suffered with recurring attacks of a similar nature at irregular intervals, varying from three to seven weeks. Her appendix was removed three years ago and a tonsillectomy was performed last year. However, the pain has increased in severity and before operation was present practically all of the time, so that her sleep had been seriously disturbed. Large meals, coarse food, fatigue and emotional upsets were thought to precipitate painful attacks. Such cases gradually develop more and more of the symptoms described with the toxic cases.

The second or toxic group present the general picture which we all recognize as neurasthenia with indigestion, especially characterized by flatulence. Chief among these manifestations are fatiguability, nervousness, palpitation, tachycardia sometimes, headache often, occasionally migraine, insomnia and mental depression. These symptoms frequently overshadow the gastric picture.

The gastrointestinal symptoms may be described as follows: From one-half to two hours after meals a sensation of weight or fulness or oppression is felt in the pit of the stomach. This is referred to as gas and if belching can be induced some relief follows. Many take bicarbonate of soda for this purpose and some find relief by an enema. Headache, nausea, nervousness and depression often accompany this indigestion. There is no distress when the stomach is empty and those who take little for breakfast may have no discomfort until after lunch. Large meals and coarse food cause more distress. Most of these patients have actual pain occasionally, but it is not very severe. Nausea is frequent and in some is almost constant. Most patients vomit occasionally, especially after physical exertion or mental fatigue. Blood is never vomited. Heartburn and pyrosis are only occasionally noted. Moderate loss of weight is usual and in some becomes considerable.

Constipation is the rule and it is often severe, most cases having always been constipated. This is sometimes relieved by attacks of diarrhea, and mucous colitis was noted in six cases. Examination of the stools reveals nothing characteristic. Mucus is usually in excess but blood is not found. Carbohydrate fermentation is more frequent than protein putrefaction, though either may occur. The bacterial flora may be changed accordingly but has no diagnostic significance.

The gastric contents are not characteristic though very marked hyperchlorhydria has been found in a few instances. A moderate degree of secondary anemia is usual and in a few cases the anemia has been severe.

Physical examination reveals a flabby, nervous patient with sallow

skin and poor muscle tone. The reflexes are oversensitive and vasomotor irritability is evident. Palpation of the abdomen usually, but not invariably, elicits tenderness just to the right of the median line and about midway between the costal margin and the umbilicus. In some the pressure of clothing is quite uncomfortable. The cecum is usually distended and sometimes thickened and tender, the result of back-pressure from spastic contraction of the sigmoid colon or, as I shall subsequently describe, it may result from accompanying bands in the ileocecal region or ascending colon.

While abnormal fixation of the duodenum should be suspected from the symptoms above described, the diagnosis chiefly depends upon roentgenological examinations with an opaque meal. Observations with the fluoroscopic screen are more satisfactory and elicit more direct evidence than do films, but both methods should be utilized. To be certain of the degree of movability of the duodenum by films only, it is necessary to make a considerable number of exposures with the patient in various positions.

Upon roentgen-ray examination a fish-hook type of stomach is usually found. The steer-horn type is occasionally observed and it is difficult to demonstrate fixation of the duodenum in such cases. There is accumulating evidence which suggests that all such stomachs are accompanied by and due to peritoneal bands, but I am not yet certain of it. The pyloric end of the greater curvature frequently presents a prognathian contour and this is very suggestive of duodenal fixation. The pylorus is found distinctly further to the right than normal and very high, generally opposite the first or second lumbar vertebra. The duodenal cap often fills slowly, apparently because of spasm, and when filled is usually dilated. The first portion of the duodenum is also moderately dilated and it characteristically passes to the left and upward. The so-called hepatic flexure of the duodenum at the junction of the first and second portions is also very high, just under the liver, and its upper margin and the descending limb of the duodenum are often flattened by pressure against the liver. The apex of the duodenum is firmly held in a position which allows no lateral movement and little or no up and down displacement, except with respiration. The sharp angulation in such cases gives the appearance of a soft tube suspended on a hook. Passage of the opaque meal is often delayed at the apex of the duodenum but it passes on in a normal manner after a few minutes. In other cases the duodenum represents three sides of a square with the upper portion lying quite horizontal, held up against the liver, flattened and firmly fixed.

While there is always some obstruction at the point of fixation, it is relatively slight. The stomach almost always empties on time and in only three of my cases was there definite gastric dilation. The tone of the peristaltic waves is good and in a few instances there

has been hyperperistalsis; such cases have at operation showed hypertrophy of the musculature.

The condition is very frequently overlooked by roentgenologists, usually because they are not familiar with it and therefore do not look for it. Some do not use the fluoroscopic screen enough and also make too few films to demonstrate it clearly. The points which I have mentioned must be kept in mind and searched for. It is also important to make observations with the patient in various positions and with varying degrees of pressure upon the epigastrium by the hand or by air cushions. By careful study an accurate diagnosis can be made in a very high percentage of cases.

The conditions for which hepatoduodenal bands are usually mistaken are cholecystitis with adhesions to the duodenum, duodenal ulcer or chronic appendicitis. Two-thirds of my surgical cases had previously had an appendectomy. If the gastric symptoms are not very severe, they have been considered neurasthenic or diagnosed chronic colitis with intestinal intoxication. In the painful cases attention is naturally centered upon the gall-bladder. The pain is, however, never so severe as that of biliary colic, seldom requiring the use of morphin, and the early age at which symptoms usually begin, together with the roentgen-ray findings, serve to differentiate. Periods of remission are frequently noted early in the history, but the symptoms eventually become quite continuous and lack the periodicity and hunger-pains that characterize peptic ulcer. Blood is not found.

While it is obvious that surgery offers the only means for removal of this condition, I wish to emphasize the fact that it is by no means necessary to operate upon all cases in order to relieve the symptoms. In my experience fully half of them can be more or less permanently relieved by medical means. It is a difficult problem to decide which patients shall be operated upon and a decision must be based upon numerous factors. Fortunately the condition is not in itself lethal nor are the effects rapidly progressive, so that one is justified in exhausting medical measures before advising an operation. The following points should in any case be considered: (*a*) The degree and extent of the duodenal fixation; (*b*) evidences of back-pressure; (*c*) severity of the symptoms, including the state of the nervous system; (*d*) the age of the patient; (*e*) whether proper medical treatment has been instituted and its effect; (*f*) the type of case, whether painful or toxic. If the patient has suffered for many years, becoming more and more incapacitated, and, as in many instances, has been on a rational regime for months or years without relief, then operation should be undertaken at once; also those cases which suffer with frequent, or more or less constant, pain and in whom the roentgen-ray evidences are marked, particularly with signs of back-pressure, should be operated upon. Mild cases, especially the toxic ones, with no delay in the passage of barium, little impairment of

strength and nutrition and with stable nervous systems, should be given a trial with medical treatment. If the response is not prompt and improvement easily maintained, they should then be operated upon, for otherwise they will almost certainly gradually decline in health and efficiency. I am more inclined to advise operation in the young patients of twenty years or so than in those at middle life, for the reason that they make a very prompt and permanent recovery, and I believe that if the condition remains unrelieved they are prone to lapse into chronic semi-invalidism as the increasing stress of life tends to aggravate the digestive and nervous systems. It is, however, difficult to estimate what the effects may be after a period of years and this I think depends a great deal upon the inherent quality of the nervous system. If the heredity is good and the nervous system stable, one is justified in longer delay than when the opposite picture is presented. When the nervous system is seriously deranged, it is better to proceed with the operation immediately, rather than to attempt to improve the general condition before operating, for I believe that in such cases the duodenal lesion is the exciting cause for the nervous derangement.

Medical treatment is often highly satisfactory. It consists in giving a diet which is non-irritating in both its chemical and mechanical constituents. All foods should be thoroughly cooked, finely divided and simply prepared and they should be given in small quantities and at frequent intervals. After the heavier meals at least, patients should lie down for an hour with the hips elevated. Due regard should be given to disturbances in gastric secretion. Many of the symptoms are due to pylorospasm as well as spasm of the duodenum itself and relief is often obtained by a mixture of belladonna and a bromide administered before meals or by benzyl benzoate given after meals. These are also useful in overcoming spasm of the sigmoid colon, which is quite constantly an accompaniment of spasms elsewhere and which is the usual cause of the constipation. A most important and fundamental point in treatment is to restore the tone of the supporting muscles and to elevate the stomach in order to relieve traction upon the point of duodenal fixation. This is accomplished by wearing an abdominal belt when in the upright position and by exercise, massage, etc., to restore the muscles in question. The operative procedure consists in simply dividing the band which, by releasing the duodenum, allows it to assume its normal position and contour. It is of course very important to suture carefully all cut and torn peritoneal surfaces, in order to limit the formation of adhesions as much as possible. Some surgeons place a layer of rubber tissue between the cut surface, leaving it in for two or three days to prevent adhesions. A transverse right rectus incision is advocated by Alfred S. Taylor who has operated on some two hundred cases. It gives ready access to the pyloric region and also to the right iliac fossa and if adhesions follow,

as is always probable, they will perhaps be in a more favorable position than when a vertical incision is made. About ten days after operation massage of the abdomen should be commenced to mobilize possible adhesions and improve the tone of the abdominal and intestinal muscles. A bland, low-residue diet is ordered for about three months, after which a coarse diet may be substituted. Constipation is invariably lessened, and often entirely relieved within a few weeks.

My experience in these cases again emphasizes the importance of exploring every abdomen which is the seat of chronic disease, whenever it may be opened; observance of this rule would obviate many subsequent operations. I have come to regard a previous appendectomy as a typical feature of this group of cases and it has almost invariably been done for so-called "chronic appendicitis." Twenty-eight of my 39 operated cases had had their appendices removed previously. Reference to Bryant's statistics shows that 40 per cent have other peritoneal bands, most of them in the right side of the abdomen; these should of course be sought for and relieved when operating. Although associated with a hepatoduodenal band, they may be chiefly responsible for the symptoms and in some cases it is impossible to conclude which band has been of most importance. In any event they should all be relieved as far as possible. I have no doubt that in some of my cases pericolic membranes have played a large part in the symptomatology.

The results of operation have been exceedingly satisfactory and I know of no abdominal condition which offers a greater assurance of relief by surgery. Those patients who suffered attacks of pain or painful distress in the epigastrium have been absolutely, and usually immediately, relieved. Symptoms referable to the stomach have generally ceased; they are always much improved. Constipation has invariably been helped and frequently cured. Vasomotor instabilities and the so-called neurasthenic symptoms have always improved, though a longer period is naturally required than to secure relief from the digestive symptoms. It is a very striking fact that the shorter the history of well-marked symptoms, the more perfect and more immediate the cure. Every one of my patients whose history was less than five years in duration is in perfect health. This group is chiefly, though not wholly, composed of young patients and it offers another reason for operating more freely and sooner in the young than in the middle-aged or old people. It is very difficult to foretell how complete will be the relief in any given case, and I have been amazed at the remarkable improvement which has followed operation in some of my older patients. It is, however, true that the least satisfactory results have invariably been in patients over forty years of age.

The maximum results from operation often do not occur for at least one, and sometimes for two years, and it is exceedingly impor-

tant to keep patients under treatment, which is chiefly dietetic and gymnastic, until they are cured.

Summary. 1. Congenital bands in the abdomen are much more frequent and of greater clinical importance than is generally recognized.

2. A study of 39 cases of the hepatoduodenal type, which came to operation is reported.

3. While fully half of this type of cases can be more or less permanently relieved by medical means, the results of operation have been exceedingly satisfactory. Surgery should undoubtedly be utilized in selected cases.

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OBSERVATIONS ON THE HEMOHISTIOBLAST OF FERRATA.

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In the course of certain pathological processes a growing literature attests that latent potentialities of the connective tissues may become manifest by their differentiation into various types of blood cells, as granular and non-granular leukocytes.*

Important evidence in support of this view has recently been advanced by Ferrata and Franco,[10] who observed in the peripheral blood and in the spleen of patients suffering from chronic myelogenous leukemia, a type of cell ("hemohistioblast") which had not been recognized as a distinct circulating form in the previous hematological literature. Morphologically, this cell has been identified with the group of tissue cells variously known as "clasmatocytes" (Ranvier), "resting wandering cells" (Maximow), "adventitial cells" (Marchand), "reticulo-endothelial system" (Aschoff), "hemohistioblasts" (Ferrata), and so forth. Not only

* In the normal adult, the hemogenic activities of the connective tissues are probably confined to the production of some of the monocytes of the blood. The formation of cells other than those normally produced is generally referred to as "metaplasia."

were these cells found in the peripheral circulation, but the presence of typical neutrophilic and eosinophilic granules in their cytoplasm indicated that the connective tissues from which they came were undergoing myeloid transformation. Subsequently, Ferrata[8, 9] described these cells in greater detail, dividing them into definite groups according to the type of granules and other characteristics which they presented.

Meanwhile Ferrata and Negreiros-Rinaldi[11] described the same cells in a case of malaria, noting that they differentiated into monocytes and lymphocytes.

Gasbarrini[13] found hemohistioblasts in lymphatic leukemia, and Reitano[20] in monocytic leukemia, in which cases they differentiated into lymphoid and monocytoid cells instead of into granular leukocytes.

Hemohistioblasts have been reported by Franco[12] in Leishmania infantum, in which they play an important part in the splenic pathology.

Esposito[6] reported 5 cases of myelogenous and 3 of lymphatic leukemia, in which hemohistioblasts were found. His illustrations picture cells in stages of myeloid and of lymphoid differentiation.

Ferrata also ascribes to the hemohistioblast the potential capacity for differentiation into red blood cells. According to his conception of pernicious anemia, for example, there is in that disease a direct derivation of megaloblasts or primitive erythroblasts from hemohistioblasts.[7] Direct evidence of this derivation has been reported by Vasiliu,[23] who found hemohistioblasts in the peripheral blood of an infant with pernicious anemia, and observed stages in their differentiation into megaloblasts. Di Guglielmo,[5] in a study of the blood of mammalian embryos, concluded that the earliest (prehepatic) circulating blood cells arise in the same manner, and calls attention to the similarity in nuclear structure between the primitive megaloblasts and hemohistioblasts. Vasiliu also noted hemohistioblasts in the normal embryo, reporting their presence in in the bone marrow of a human embryo of seven months' gestation.

The importance of the diffuse connective tissue in the pathogenesis of a number of diseases in which skin lesions are associated with changes in the hematopoietic organs, has been emphasized by Bétancès,[1] who believes that in these conditions, which he groups among the "maladies de l'hematopoièse," the hemohistioblasts are capable, when irritated, of directly giving rise to granulocytic and lymphoid cells, without necessarily passing through the hemocytoblast stage.

In these several articles the hemohistioblasts are represented as "veri elementi mesenchimatici embriali," comprising a diffuse hematopoietic tissue, which, in morbid processes, undergoes transformation into specific blood cells.

The author has observed hemohistioblasts in 4 cases of chronic

myelogenous leukemia, and 1 case each of lymphatic leukemia, quartan malaria, infantile anemia of von Jaksch, and Staphylococcus aureus septicemia.

Blood smears were stained with Wright's stain or the Jenner-Giemsa combination, and by the peroxydase method. For the latter a solution of benzidine in methyl alcohol to which a drop of hydrogen peroxide had been added, was used as recommended by McJunkin,[17] and the preparation counterstained with Wright's stain. By this method all structures which do not give a positive reaction are stained as they normally are by Wright's stain.

The 4 cases of myelogenous leukemia were typical—clinically and hematologically. The total white counts on admission were between 90,000 and 600,000, of which hemohistioblasts constituted a small and variable percentage—not over 5 per cent. Transitional stages were observed between undifferentiated forms and those with typical neutrophilic or eosinophilic granules. In 1 of these cases, which has been followed over a period of about eight months, hemohistioblasts have been constantly present in the blood, although the total leukocyte count has at times been brought within normal limits by roentgen-ray treatment.

The case of lymphatic leukemia was atypical, corresponding to the "leukosarcomatosis" of Sternberg. The patient, a boy, aged thirteen years, was acutely ill with fever, cough, left hemothorax, lymphatic and splenic enlargement, and had on admission a sublymphemic blood picture—from 16,000 to 22,000 white cells, with 65 per cent lymphocytes of normal morphology. This blood picture persisted for several weeks. About two weeks before death the white cells rose to 100,000, of which over 90 per cent were atypical lymphoid cells, frequently of the Rieder type. At this time hemohistioblasts were found, though rarely, in the circulation. They contained typical eosinophilic granules—an interesting feature, as the hemohistioblasts previously reported in lymphatic leukemia were of the lymphoid variety. Necropsy disclosed a mediastinal mass in the region of the thymus, involving the left pleura and pericardium, with generalized lymphatic enlargement. Microscopically, the tissues showed the diffuse lymphoid lesions usually found in lymphatic leukemia.

The patient with quartan malaria was acutely ill, and died less than two weeks after the onset of the first symptoms. Jaundice was marked, and there was increasing lethargy, pulmonary congestion and leukocytosis (22,800), with numerous abnormal monocytes, plasma cells and other pathological lymphoid forms. Quartan parasites were numerous. The hemohistioblasts in this case were of the monocytoid and lymphoid forms, and were frequently phagocytic.

In the case of Staphylococcus aureus septicemia the hemohistioblasts were also monocytoid and lymphoid, and were phagocytic for bacteria. As a terminal event, cells containing as many as

twenty cocci in various stages of intracellular digestion appeared in the circulation. The diagnosis in this case was confirmed by repeatedly positive blood cultures.

In von Jaksch's anemia the hemohistioblasts contained typical myeloid granules.

Morphology of the Hemohistioblasts. The colored illustrations of Ferrata and his collaborators excellently depict the characteristics of the hemohistioblasts. In general the cells are of very large size, irregular shape, possess a single round or oval nucleus with a characteristic reticulated internal structure, likened by Ferrata to a sponge. They have distinct nucleoli, and basophilic cytoplasm in varying amount, with or without granules. Attenuated cytoplasmic prolongations of considerable lengths may extend between other cells of the smear and give rise to bizarre forms. In some instances mitotic figures have been observed. These general characters are modified in the course of subsequent differentiation.

The hemohistioblasts may be conveniently divided into four main groups:

I. Undifferentiated Hemohistioblasts. These represent the undifferentiated histogenous cells. Their nuclei are distinctly different from those of any normal cell of the blood or the immature parenchyme cells (hemocytoblasts) of the blood-forming organs. The cytoplasm may be non-granular (Figs. 1 and 4), or may contain azurophilic granules and filaments (Figs. 2 and 3). The filaments are fine attenuated azurophilic structures of varying lengths, which Ferrata identifies with mitochondria. Transitional stages may be observed from undifferentiated forms to hemocytoblasts, or directly to granular leukocytes, lymphocytes and monocytes.

II. Lymphoid Hemohistioblasts. This group includes cells with basophilic cytoplasm devoid of granules, and with nuclei which approach those of normal lymphocytes. They represent stages in the transformation of the undifferentiated forms to lymphocytes.

III. Monocytoid Hemohistioblasts. All stages of differentiation from hemohistioblasts to monocytes are found. The cytoplasm is basophilic, and may contain azurophilic granules of the type found in monocytes. These cells are frequently phagocytic, as observed in cases of malaria and in septicemia. It is possible that the "macrophages" reported by various authors and experimentally produced by Simpson[22] belong in this group, and indicate a mobilization of connective-tissue elements.

IV. Myeloid Hemohistioblasts. The greatest variety is found in this group. In cases of chronic myelogenous leukemia the following subvarieties may be distinguished:

1. Undifferentiated forms, as in Group I.

2. Cells similar to the above, but containing premature granules of either neutrophilic or eosinophilic type, with or without the presence of typical mature granules as well (Fig. 5). These imma-

ture granules are more or less basophilic in their staining properties (Naegeli,[18] Ferrata,[8, 9] Jolly[15]). The cytoplasm begins to lose its basophilic quality, especially in the perinuclear zone, where the weakly acidophilic hyaloplasm appears.

FIG. 1

FIG. 2

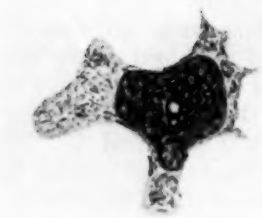

FIG. 3

FIG. 4

FIGS. 1 to 4.—Undifferentiated hemohistioblasts.
FIGS. 2 and 3.—Contain azurophilic filaments and granules.

FIG. 5

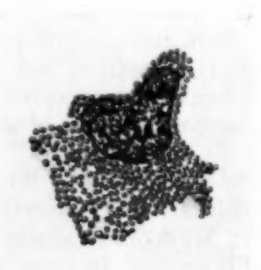

FIG. 6

FIG. 5.—Hemohistioblast with eosinophilic granules, early stage. Several of the granules are immature. Nucleoli are present.
FIG. 6.—Hemohistioblast with eosinophilic granules, late stage. The granules are all mature. There are no nucleoli.

3. Cells with typical neutrophilic or eosinophilic granules. The nucleoli, which are conspicuous in the younger forms, have disappeared. The nuclei in general maintain their sponge-like character, by which they may be distinguished from ordinary myelocytes,

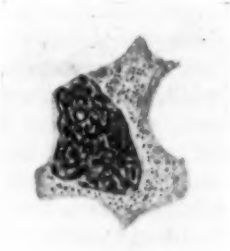

FIG. 7

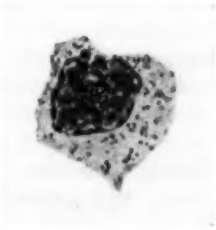

FIG. 8

FIG. 7.—Hemohistioblast with neutrophilic granules.

FIG. 9

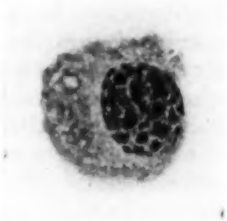

FIG. 10

FIGS. 8 and 9.—Monocytoid hemohistioblasts with azurophilic granules.
FIG. 10.—Lymphoid hemohistioblast. From case of malaria.

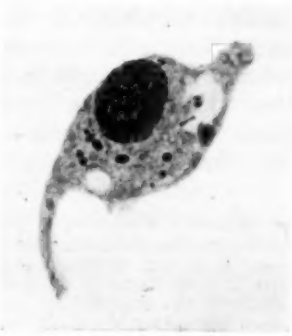

FIG. 11

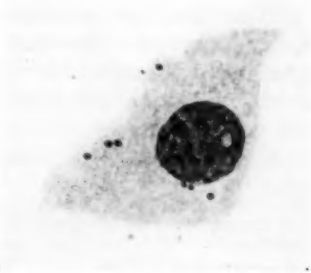

FIG. 12

FIG. 11.—Hemohistioblast containing malarial pigment.
FIG. 12.—Monocytoid hemohistioblast from case of septicemia, containing several phagocytosed bacteria.

The illustrations were drawn with the aid of a camera lucida from blood smears stained by Wright's or Jenner-Giemsa stains, at a magnification of 1000 diameters.

even when the amount of cytoplasm is greatly reduced and the cell approaches them in size (Figs. 6 and 7).

In each of these groups are found cells in which the nuclear and cytoplasmic characters vary in degree, indicating successive stages in differentiation.

Fragments of the cytoplasm of hemohistioblasts are frequently found in myelogenous leukemia. They vary in size from that of blood platelets to fragments larger than ordinary leukocytes. They may resemble platelets or polychromatophilic red cells, with which they should not be confused (Castronuovo[3]). In some instances they contain neutrophilic or eosinophilic granules, or azurophilic filaments, in which cases they may be easily distinguished.

The Oxydase Reaction. The results obtained with the benzidin oxydase stain correspond in every detail with the author's observations with this method on other types of blood cells: in every positively reacting cell the oxydase is apparently confined to the cytoplasmic granules; in every cell devoid of granules the reaction is negative.*

Not all granules, however, give a positive reaction. Those which react positively are the neutrophiles, eosinophiles and the azurophilic granules of monocytes, myeloblasts† and hemohistioblasts. The granules which react negatively are the basophiles,‡ the immature basophilic granules of eosinophiles,[14] the metachromatic granules of blood platelets and megakaryocytes and the azure§ granules of lymphocytes.

These results suggest that the oxydase reaction depends upon the type of cell, rather than upon its origin in any particular organ or tissue.

The hemohistioblasts represent a definite type, not to be confused with any other cell of the peripheral blood. Their morphology, especially the characteristics of nuclear structure, is that of connective tissue (mesenchymatous and endothelioid) cells generally. That they are not degenerative forms is evident from their perfectly preserved structure, and their differentiation through progressive, not regressive stages. Their specific characters are gradually acquired, not gradually lost. This is particularly well

* Naegeli[19] and others report positive oxydase reactions in non-granular "myeloblasts." The author's observations corroborate the previous work of Rosenthal[21] and of Jolly,[16] who states, "Les oxydases paraissent appartenir seulement aux leucocytes granuleux. Les lymphocytes, leucoblastes et myéloblastes ne donnent pas ces réactions."

† Myeloblasts of Ferrata; unripe myelocytes (promyelocytes) of Naegeli.

‡ Some observers report a positive reaction in basophiles.

§ Naegeli distinguishes between the "azure" granules of lymphocytes and the "azurophilic" granules of other cells. Jolly and others do not make this distinction. The results of the oxydase reaction show that all granules stainable with azure-eosin mixtures are not identical. In normal blood, for example, the granules of monocytes, when present, react (weakly) positively, while those of lymphocytes react negatively and stain as they normally do with Wright's stain.

illustrated in the myeloid types, in which the few granules which first appear are immature,* as evidenced by their staining reactions.

Discussion. The term "hemohistioblast," as used by Ferrata, refers to the indifferent polyvalent cells diffusely situated in the connective tissues, commonly known as "clasmatocytes," "resting wandering cells," etc.

The presence of hemohistioblasts in the peripheral blood in the cases herein discussed, and their differentiation into leukocytes and lymphocytes indicate that these blood cells were being formed directly from connective tissue, without the usual intermediate hemocytoblast stage. There was, in other words, a connective-tissue "metaplasia."

True metaplasias of all kinds are due to changes in the environment in which the cells live.[2] The importance of environmental factors in the initial (heteroplastic) stages of hematogenesis has received special attention by Danchakoff,[4] who states: "On the basis of descriptive histogenetic studies it seemed plausible to admit that environment can modify isolated cells; that the metabolic processes of the cells are the resultant of their physicochemical constitution plus physicochemical conditions of the environment (of course hormones, enzymes and so forth are included in the environment), and do not depend exclusively upon their physicochemical constitution; that different substances arise in the cell body (hemoglobin, various specific granules) in polyvalent cells as result of changes, determined by differences in the environment. The existence of cells endowed with various potencies has in consequence been largely admitted. The specificity of the various mature blood cells would thus be brought about by factors extrinsic to the stem cells."

Observations on the organs in leukemic and other conditions have led several authors to the conclusion that the metaplasias occurring therein arise by the local proliferation of histogenous cells, under the influence of extrinsic factors. A detailed discussion of this subject will not be undertaken here. It should be emphasized, however, that the identification of the hemohistioblast as a histogenous cell, and the development within its cytoplasm of specific leukocyte granules, admit of only one interpretation—the connective tissues undergo "metaplasia" by direct differentiation of their cells.

Environmental factors are thus of the same importance and significance in postnatal metaplasias as in embryonic differentiation. Inasmuch as hemohistioblasts acquire the characters of

* Graham[14] considers that the basophilic leukocyte of the blood is a degenerating eosinophile, and these basophilic granules which eosinophiles sometimes contain, are a sign of degeneration rather than immaturity. In the present investigation, however, the presence of other signs of immaturity (basophilic cytoplasm, fewer granules, less differentiated nuclear structure, presence of nucleoli and sometimes of mitochondria), indicates that the cells in question are less mature than those containing only eosinophile granules.

specific blood cells, we must assume that they were potentially capable of this differentiation, although this potency had been latent; and as the type of differentiation is not the same in all cases, the cells must be capable of differentiation in more than one direction, that is, they are "multipotent." Furthermore, when identical cells develop in diverse directions the cause of their differentiation cannot be intrinsic, but must be sought in differences in their environment.

Conclusions. 1. The hemohistioblasts of Ferrata (clasmatocytes, adventitial cells, resting wandering cells, reticulo-endothelial cells, etc.) play important hemocytogenic role in myeloid and lymphoid "metaplasia" in various conditions.

2. In pathological processes these cells and their derivatives may appear in the peripheral blood stream.

3. Hemohistioblasts are potentially capable of differentiation into granular leukocytes, lymphocytes and monocytes.

4. The type of differentiation which they undergo is not dependent upon intrinsic cell differences, but is determined by the character of the environmental conditions imposed.

5. A positive oxydase reaction is given by hemohistioblasts only if they contain neutrophilic, eosinophilic or azurophilic granules.

NOTE.—The cases presented in this paper were observed in the medical wards of Bellevue Hospital. Grateful acknowledgment is made of courtesies extended by Drs. Van Horne Norrie, Charles E. Nammack, Theodore J. Abbott, Eugene F. Du Bois and Herbert B. Wilcox, in permitting the author to study and report observations of cases on their respective services.

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LUNG ABSCESS.

Report of Thirty-three Cases.

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The incidence of lung abscess has apparently been on the increase during the past decade. From what causative factors this is due we can only conjecture. There seems to be a rather general impression that the greater frequency of nose and throat operations under general anesthesia has had something to do with this increase. The last great pandemic of influenza has had perhaps some influence.

In the present study there are 33 cases of lung abscess. Fourteen cases were selected from our personal records and 19 from the records of the Baptist Hospital and the St. Joseph Infirmary. All of the cases have occurred during the last five years.

Etiology. The Staphylococcus aureus was the predominating organism in the sputum. Anerobic bacilli, especially the gas bacillus, have been reported. Twelve cases (36 per cent) followed operative procedures under general anesthesia. Of these, 4 were from operations other than on the throat, 1 from a ruptured duodenal ulcer, 1 from mastoid disease, 1 from carcinoma of the bladder, and the other followed tooth extraction. Seven cases followed tonsil operations, all under general anesthesia. It is significant that 75 per cent of the postoperative cases followed operations on the throat and mouth. In 33 per cent influenza was responsible, in 15 per cent pneumonia, in 2 per cent an infection of the hand, in 2 per cent an injury to the chest wall, and in 12 per cent the etiology was unknown. Therefore, in 64 per cent of the lung abscesses in this series the etiology was from non-operative causes.

TABLE I.

POSTOPERATIVE.	Cases.	NON-OPERATIVE.	Cases.
Tonsil	7	Influenza	10
Mastoid operation	1	Pneumonia	5
Fractured jaw	1	Unknown	4
Ruptured duodenal ulcer	1	Injury to chest	1
Carcinoma of bladder	1	Infection of the hand	1
Tooth extraction	1		
Total	12	Total	21

Sex. Males seem to be more often affected than females. In our series there were 17 males and 16 females.

Age. The ages varied from four to fifty-five years. All of the postoperative cases were adults. The greater number of cases occurred in patients of the second or third decade of life.

Location. There was a predilection for location of the abscess in the lower lobes and especially the right lower lobe. This was particularly evident in the postoperative group, of which 75 per cent were in the lower lobes and 50 per cent were confined to the right lower lobe. In the non-operative cases 71 per cent were found in the lower lobes, 38 per cent being in the right lower lobe and 33 per cent in the left lower lobe. The location of the abscess was in the lower lobes in all cases and 75 per cent were in the right lower lobe following tonsil and mouth operations. Because the throat operations were done under general anesthesia, the aspiration hypothesis must be strongly considered. In Jackson's series 62 to 75 per cent of foreign bodies were found to have entered the right primary bronchus. He gave as reasons for this localization the following:

1. The greater diameter of the right primary bronchus; (2) the smaller angle of deviation of the right primary bronchus from the trachea; (3) the situation of the carina to the left of the axis of the trachea; (4) the action of the trachealis muscle; (5) the greater volume of air going into the right primary bronchus.

TABLE II.

POSTOPERATIVE.	Cases.	NON-OPERATIVE.	Cases.
Right lung:		Right lung:	
Upper lobe	1	Upper lobe	1
Middle lobe	1	Middle lobe	2
Lower lobe	6	Lower lobe	8
Left lung:		Left lung:	
Upper lobe	1	Upper lobe	3
Lower lobe	3	Lower lobe	7
Total	12	Total	21

TABLE III.

ALL CAUSES.

	Cases.
Right lung involved	20
Left lung involved	14
Lower lobes involved	23
Upper and middle lobes involved	11
Right lower lobe involved	13
Left lower lobe involved	10
Total	91

AS TO CAUSE.

POSTOPERATIVE.		NON-OPERATIVE.	
Right lung involved	7	Right lung involved	13
Left lung involved	4	Left lung involved	9
Lower lobes involved	9	Lower lobes involved	13
Upper and middle lobes involved	2	Upper and middle lobes involved	9
Right lower lobe involved	6	Right lower lobe involved	7
Left lower lobe involved	3	Left lower lobe involved	6
Total	32	Total	57

Moore has reported 202 cases of lung abscess from information derived from questionnaires sent to other throat specialists. Of these no localization was stated in 91 cases. Of the remaining 101 cases, the middle and upper lobes were involved in 32 per cent, the lower lobes in 60 per cent, the right side in 63 per cent, the left side in 27 per cent. This showed a predilection for the localization of the abscess in the right lower lobe. Reports from the current literature are not uniform as to the right lower lobe being the most frequent location for pulmonary abscesses following throat operations. Lemon, Whitemore and Wessler have reported a series of cases in which there were more abscesses in the upper lobes than in the lower lobes following throat operations. In fact, Wessler found the upper lobes twice as often involved. However, the concensus of opinion is that the lower lobes, and principally the right lower lobe, are the favorite locations for pulmonary abscess. In our series of cases there was a decided tendency for the basal lobe, especially the right, to be the place where the abscess most frequently occurred, and this was more apparent in the postoperative than in the non-operative group.

Certain anatomical facts suggest the reasons why the right lower lobe is involved more often in postoperative lung abscess than are other lobes. Heretofore, we have given Jackson's reasons, and they are probably sufficient. However, for further emphasis we shall call attention again to additional outstanding factors. The right primary bronchus rises nearer to the trachea than does the left primary bronchus; it is shorter, wider, and runs downward in a more vertical course; it lies more in line with the trachea, the angle with the median line being 24.8°, whereas, there is an angle of 45.6° between the trachea and the left primary bronchus. The first

branch to the right upper lobe leaves the main stem 1 inch from the trachea, and the first branch to the left upper lobe leaves its main stem 2 inches from the trachea.

Proponents of the aspiration hypothesis are not without opposing arguments favoring embolism as the route for the development of pulmonary abscess. A study of the pulmonary arteries shows that practically the same facts are found to be present as those described regarding the location of the bronchi, because the distribution of the pulmonary arteries is practically the same as the distribution of the bronchi. The pulmonary artery rises from the anterior left angle of the base of the right ventricle at the termination of the conus arteriosus. It is 2 inches long and divides into a right and a left branch. The right branch is lower and larger and descends with the main bronchus to the lower part of the right lung and sends a large branch to the right upper lobe. The left branch is shorter, smaller and occupies a higher position than the right branch.

The lymph glands of the thorax form five named groups with subdivisions: The sternal, the intercostal, the anterior and the posterior mediastinal and the bronchial groups. It is unlikely that infection could travel from the tonsils to the superior deep cervical glands, whose efferents normally pass to the inferior deep cervical glands, and thence to the jugular lymph trunk, and be carried into the lung tissue. In fact, such a course seems to be an impossibility. Van Zwalenburg and Grabfield have shown an association of the pleural cap with early pulmonary tuberculosis and tonsillar tuberculosis. If their ideas are correct, we have an explanation for the extension of bacteria from diseased tonsillar tissue to the upper lobes of the lungs and thence to the lung hiluses.

It is interesting to note that R. H. Babcock found in 1500 cases of lobar pneumonia that the right lung was involved in 52 per cent the left lung in 35 per cent, and the right lower lobe in 33 per cent, or twice as often as any other single lobe. Haberfeld in 68 autopsies on cancer of the lung found that the right lung was involved in 65 per cent, the left lung in 35 per cent, and that, especially the right lower lobe was the more frequent location for the disease. Rupp, in a series of cases of pulmonary embolism, found that the right lung was affected in 61 per cent in comparison to 39 per cent in the left lung. From these considerations it would seem that other diseases, namely, pneumonia, cancer and embolism attack more frequently the right lower lobe than they do any other part of the lungs. The anatomical position of the right pulmonary artery and the right primary bronchus, and the greater volume of air in the right lung, which is 10 per cent larger than the left lung, causes a greater wear and tear on the right lung than on the left lung. In our opinion these anatomical facts do not disprove the aspiration hypothesis for postoperative lung abscess; they merely point out other avenues for consideration, although much of the accumulated data up to this date points favorably to the idea that aspiration is the

most frequent cause for lung abscess following throat operations under general anesthesia.

Clinical Features. The onset of lung abscess varies from a few days to three or four weeks, and may be abrupt with a hard chill or may follow a period of less pronounced symptoms, such as, malaise, slight fever, pleuritic pain, and dry cough. The acute stage may be fulminating. The patient at first is ofttimes quite septic with high fever, which is subject to decided diurnal fluctuations, the typical step-like fever of sepsis. Chilly sensations and sweating are noticeable, and at times distinct rigors. The cough at first is dry and harassing but, later, is followed by the paroxysmal expectoration of very foul, purulent, occasionally blood-tinged sputum. Sometimes severe pulmonary hemorrhages occur. One of our patients had a copious hemorrhage. The patient may go for hours with little or no expectoration and, then, expectorate from 3 to 8 ounces of very foul sputum. The odor, although not as bad as in cases of pulmonary gangrene, may seem to pervade the whole room. As a rule the patients lie more comfortably on their backs, slightly propped up, and are unable to lie on either the one side or the other. The sputum is purulent and does not separate into three layers on standing as it does in bronchiectasis. Elastic fibers are often found, but their absence means nothing contrary to the diagnosis of lung abscess. There may be some complaint of pleuritic pain. During this acute stage the patient looks sick and prostrated. The pulse and respiration are increased, although the latter is not increased in the same proportion as the pulse is and it is not nearly so rapid as the respiration in a lobar pneumonic patient. If the patient does not succumb during the acute stage, which varies from a few weeks to several months, a subacute stage is approached followed by a chronic stage. At this time the outstanding feature of the case is the paroxysmal expectoration of large quantities of foul-smelling sputum. It is remarkable that the patient does not always show extreme physical weakness during the chronic stage of pulmonary abscess. Of course, these patients are decidedly subnormal physically, but they maintain ofttimes usually good physical vigor. The temperature may be subnormal in the morning and rise to 99.6° to 103° F. in the afternoon. Occasionally the reverse type of temperature, with the peak in the morning, may be seen. The respiration is not greatly modified, but the pulse is moderately accelerated. There is a tendency toward frequent exacerbations of temperature, the temperature falling for a few days following the paroxysmal expectoration of large quantities of purulent sputum. Sweating and chilly sensations are usually present. Generally there is a lowering of the resistance of the patient, and he becomes sallow, loses weight and looks markedly subnormal and often quite sick. The appetite is fickle, and gastrointestinal symptoms, especially a tendency toward diarrhea, are frequently seen. A distinct leukocytosis with polymorphonuclear increase is frequently a symptom.

FIG. 1.—Pulmonary abscess involving the right lower lobe.

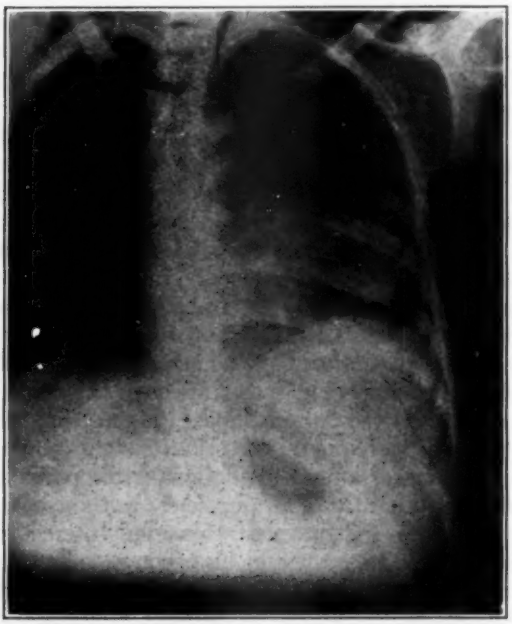

FIG. 2.—Pulmonary abscess involving the left lower lobe.

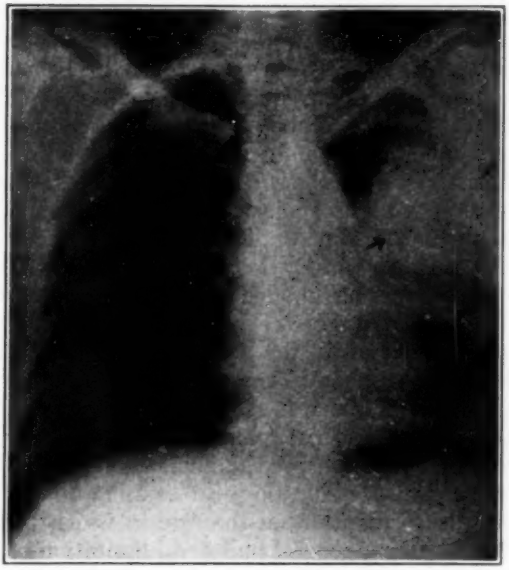

FIG. 3.—Pulmonary abscess involving the left upper lobe.

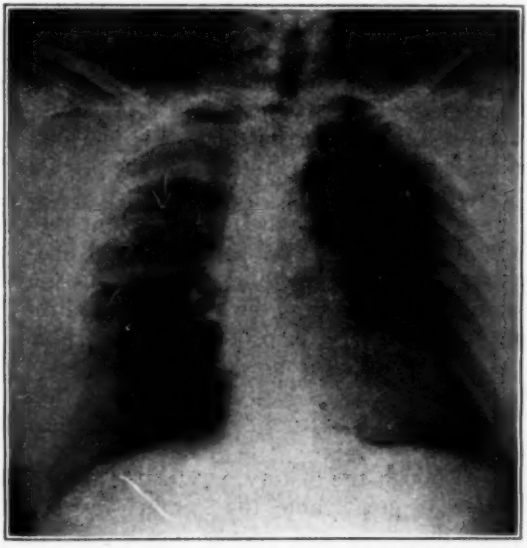

FIG. 4.—Bronchiectatic pulmonary abscess involving the right lung.

Types. Two types of lung abscesses are found: The typical solitary lung abscess and the so-called bronchiectatic lung abscess. The former is a single abscess, while the latter is formed by the fusion of smaller abscesses so that they are connected by small openings, or it may be formed by the irregular extension of a primarily single abscess so that it is then composed of several coalescing compartments. In my opinion it is unfortunate that the term "bronchiectatic lung abscess" has become so generally used because of the evident confusion with bronchiectasis, for there is no etiological similarity between the two conditions. The term "multilocular lung abscess" would more nearly describe the condition. The abscess in the subacute stage is surrounded by a zone of acutely inflammatory lung tissue. In the more chronic stage definite fibrosis takes place. When the abscess in the acute stage is near the pleura a fibrinous, pleural exudate may form, which later organizes into dense fibrous tissue bringing about firm adhesions between the parietal and visceral pleuræ. Ordinarily, however, the abscess ruptures into a bronchus and is discharged therein.

Physical Examination. The physical examination of the chest reveals usually less expansion on the side in which the abscess is located. This may be a general unilateral limitation of movement of the chest wall, or the limitation may be localized to the upper or to the lower chest, depending upon the localization of the abscess. As a rule there is less limitation of movement when the upper lobes are involved. Tactile fremitus is usually diminished over the abscess. When the abscess lies near the chest wall, as is usual when the lower lobes are involved, there may be dulness to ordinary percussion. However, when the abscess is deep-seated, and there is an area of air-containing pulmonary tissue between the visceral pleura and the abscess, light percussion may fail to reveal any dulness, and even heavier percussion may not demonstrate dulness. Generally there is a very definite increase in the pitch of the percussion note. The breath sounds directly over the abscess may be decreased. However, they may be quite harsh at the periphery of the abscess, and large moist rales may be heard in this area. In cases, which are draining through a bronchus, one may hear these large, moist rales extending from the abscess toward the hilus region of the affected side. Whispering pectoriloquy and tubular breathing are usually absent. In the chronic cases all the signs of cavity may be present over the abscess. In our experience this was rarely heard even though we knew from roentgen-ray studies that a large cavity was present.

Diagnosis. Although the history, physical examination, and the clinical course are of great value, the roentgen-ray is indispensable for the correct diagnosis and proper localization of pulmonary abscess. The bronchoscope has some slight usefulness, too.

Acute lung abscess must be differentiated from acute bronchitis,

pneumonia, pulmonary embolism and empyema. Careful consideration of the history, the clinical course, the physical signs, and roentgen-ray should easily rule out these diseases. The differential diagnosis of chronic lung abscess from tuberculosis, chronic bronchitis, bronchiectasis, lung tumors, and syphilis is more difficult than the differential diagnosis of acute lung abscess. In tuberculosis the involvement is more apical, there being frequently marked depreciation of health, a tendency toward progression of the pulmonary signs, which as a rule are absent in abscess, and there is no leukocytosis, and frequent sputum analyses usually reveal tubercle bacilli. In chronic bronchitis the lung findings are more generalized, there being less tendency to paroxysms of purulent sputum, and to exacerbation of increased temperature. Chronic bronchitis is usually secondary to some other disease, and there is no leukocytosis, and the rales are dry. In bronchiectasis clubbed fingers are more frequently observed, the sputum is more abundant and foul, the cough is more affected by posture, the sputum separates into three layers on standing, no elastic fibers are found, and there is no leukocytosis. Lung tumors and pulmonary syphilis may be excluded by the roentgen-ray.

TABLE IV.

INCISION AND DRAINAGE.	Cases.	ARTIFICIAL PNEUMOTHORAX.	Cases.	POSTURAL DRAINAGE.	Cases.
Improved	3	Improved	2	Improved	4
Recovered	3	Recovered	4	Recovered	3
Died	2	Died	6	Died	4
Unimproved	0	Unimproved	0	Unimproved	2

	Per cent.
Mortality—12 in 33 cases—36.3 per cent:	
From incision and drainage	25.0
From artificial pneumothorax	50.0
From postural drainage	30.0
Recovered:	
After incision and drainage	37.5
After artificial pneumothorax	33.3
After postural drainage	23.0

Treatment. In our series incision and drainage gave the best results, showing 37.5 per cent recoveries. Three other cases 37.5 per cent, were greatly improved making 75 per cent of the cases in which incision and drainage were performed that favorable results were obtained. The mortality after incision and drainage was less than after postural drainage alone or after artificial pneumothorax. Artificial pneumothorax was successfully used in 4 cases, 33.3 per cent, and 2 cases 16.6 per cent, were improved, making a favorable outcome in 50 per cent. The mortality, 50 per cent, however, was high. Postural drainage gave the least number, 3, 23 per cent of recoveries. Four cases, 30 per cent were improved, making a total

of 53 per cent of the cases treated by postural drainage favorably affected. The mortality, 30 per cent, was slightly higher than in the cases treated by incision and drainage but considerably less than the cases treated by artificial pneumothorax.

In the early acute cases postural drainage should be instituted, and persisted in, until after the severe symptoms have abated. If the abscess does not rupture through a bronchus, bronchoscopic drainage may be done. This will initiate drainage from the abscess into the bronchus, and will result in a prompt amelioration of the more acute symptoms. In our experience early interference by incision and drainage or artificial pneumothorax is very harmful. After the acute symptoms have passed and the abscess has become more localized a thoracotomy may be performed. Careful study of stereoscopic roentgen-ray plates, combined with physical examination, is necessary. Needling of the abscess is dangerous because of the possibility of infecting the free pleural cavity. By the use of a pneumothorax needle, attached by a tube to a manometer, the presence of pleural adhesions over the abscess may be determined. If adhesions are present, their location may be delineated by inserting the needle in the center of the dull area, and if adhesions are indicated by the absence of free manometric oscillations, the needle should be repeatedly inserted, peripherally, in all directions until free oscillations of the manometer signifies the absence of adhesions. In this way the area of adherent pleura may be very accurately indicated, and the surgeon may without fear of a secondary lung collapse, or of infecting the free pleural cavity, open into the abscess. Artificial pneumothorax should never be performed during the acute stage of the pulmonary abscess, and this is especially true when there are localized adhesions present between the parietal and the visceral pleura. For in such cases excessive coughing may tear the adhesions away from the visceral side causing a serious spontaneous pneumothorax. However, in the chronic, localized pulmonary abscess without pleural adhesions, an artificial pneumothorax may produce good results.

Summary. Lung abscess is more frequent after throat operations than after all other operations. This suggests the correctness of the aspiration hypothesis, there being also definitely known facts to support this view. However, aspiration is not the only way in which pulmonary abscess may develop for influenza, pneumonia and localized infections may be the cause of lung abscess. It may not be amiss to advise strongly against using general anesthesia for nose and throat operations on adults.

RADIUM IN DERMATOLOGY.*

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In 1896 Henri Becquerel[1] discovered radioactive substances through the medium of a burn sustained by carrying some ore in his waistcoat pocket. It was this burn that gave Pierre Curie the idea that radium might prove useful in medical work.

In 1901 Degrais and Danlos had radium put at their disposal for therapeutic purposes but it was not until 1906 that Henri Dominici actually demonstrated that therapy by radium was a reality and that various depths of tissue below the skin could be affected by a process of filtration and that such radium rays had a relatively marked innocuousness for healthy tissues up to a certain point; while, on the other hand, they preserved all their special action on neoplastic tissues.

There are three varieties of rays constantly emitted in the disintegration of radium; that is, alpha and beta electromagnetic rays and non-material electromagnetic pulsations of the other called gamma rays. Alpha rays are of short wave length and are easily filtered out with a thin layer of glass, rubber or almost any other material. Beta and gamma rays are progressively more penetrating and very hard gamma rays can be projected through several inches of human tissues and several centimeters of dense metallic substances.

Beta and gamma rays when they impinge on matter or material produce secondary rays, varying in their intensity with the density of such material, and it is believed that these are the rays responsible for the biological effect of radium on tissues.

In varying doses these rays are thought to either stimulate, inhibit or destroy the reproductive property of cells, especially embryologic cells, reproductive cells, secretory or gland cells and certain inflammatory or neoplastic cells.

In full doses to the skin radium attacks particularly elastic tissue, reproductive cells of the rete, sebaceous and sweat glands, papillæ, and the epithelial lining of the bloodvessels and blood spaces, and if excessive is capable of producing atrophy and telangiectases or even extensive burns comparable to those that can be produced by roentgen-ray.

Any attempt therefore to produce a permanent epilation of the

* Read before the Post-Graduate Hospital clinical meeting, April 11, 1924.

face in hypertricosis is only to be condemned because of the necessary atrophy that must result to these other tissues in at least some of the cases.

That normal skin tissues subjected to erythema doses of radium do tend to recover more quickly and more perfectly than from a corresponding reaction produced by roentgen-ray, I believe to be true, but this may be explained by the fact that less extensive areas are treated by radium than those for which roentgen-ray radiations are ordinarily used and there is therefore a less extensive area of blood supply cut off.

To state that radium has a selective action on certain pathological tissue is perhaps misleading but Prime[2] has established that cells devoted to rapid growth and mitosis are decidedly more easily destroyed by radiation than are normal cells which are not mitosing except for purposes of repair, and furthermore, have an adequate equipment of anatomically well formed vessels to supply them.

This explains the excellent cosmetic results that can be obtained in certain types of skin cancer by radium, the cancer cells being destroyed while normal surrounding tissue cells are temporarily inflamed and even stimulated to a process of repair.

The reason why radium is so eminently effective in certain diseases of the skin is due to the fact that we are dealing with surface lesions, most of which can be penetrated by even the hard beta rays, lying as they do within the skin thickness.

Radium placques, therefore, are eminently suited to most of the lesions and for deeper lesions extending in beneath the skin, placques combined with the insertion beneath and around the lesions of radium carrying needles, gives a crossfire method with a maximum raying of the lesion itself and a minimum amount to the skin.

Full strength placques are used from 5 mg. up to 20.52 mg. (a full strength placque is one in which each square centimeter of placque surface contains 5 mg. of radium element. A 20 mg. full-strength placque therefore covers an area of 4 square centimeters).

As the softer beta rays produce so superficial and irritating a reaction in the skin surface, they have been found to be of little use in dermatological lesions and since 1914 my placques have all had a facing of 0.1 mm. of brass soldered over the face of the placque in order to cut out these irritating superficial rays.

Practically 90 per cent of all rays emitted are alpha rays, 10 per cent are beta rays and 1 per cent are gamma rays, so that where an absolutely full strength placque will produce a mild erythema in two to three minutes, a filtration of 0.1 mm. of brass and 1 mm. of rubber will require thirty to thirty-five minutes to produce a similar erythema.

Temporary alopecia is produced by a full strength placque with a filtration of 0.1 mm. of brass and 0.1 mm. of rubber in fifty-five to sixty minutes, and permanent alopecia results from the application of such a placque for eighty to ninety minutes.

A faint while level mark will follow an exposure of one hundred and twenty minutes and a quite perceptible but level scar seems to follow such an exposure from one hundred and fifty minutes followed by more or less development of telangiectases with such a filtration.

Foerster[3] states that approximately one-half of the beta rays are filtered out by a thickness of 0.05 mm. of platinum, 0.1 mm. of lead, 0.11 mm. of silver, 0.13 mm. of brass and 0.4 mm. of aluminum.

Caldwell and Russ have determined that the intensity of the hard beta rays is reduced to about 6 per cent of their initial value after passing through 1 cm. of epithelial tissue.

One-half of the gamma rays are absorbed by 6.2 cm. of aluminum, 1.4 cm. of lead, and 1.14 cm. of silver.

The intensity of radiation is further reduced by distance, but not exactly I believe in accordance with the inverse square law, that is, doubling the distance reducing the intensity to one-fourth.

The radium needles used are mostly of 5 mg. platino-iridium with wall thicknesses of 0.2 mm. and can be left embedded in soft healthy tissue for two hours with very little reaction and in dense tissue for three or four hours or more.

Where deeper ray effects are required 0.1 mm. of brass and 5 mm. of rubber will produce only a slight skin erythema after two hours of exposure and a similar erythema will result after a six-hour exposure with a filtration of 0.1 mm. of brass, 1 mm. of aluminum and 5 mm. of rubber, with a penetration of a half inch of living tissue.

The substitution of 1 mm. of lead in place of the 1 mm. of aluminum requires an increase of exposure up to eighteen hours for the production of such a faint skin erythema, with of course a penetration of several centimeters beneath the skin.

Radium Therapy in Diseases of the Skin. Hyperkeratoses. Clavus and callosities of the feet, two types of lesions that are frequently the cause of pain and discomfort, are so comfortably amenable to treatment by radium that it must be regarded as the method of choice in these lesions.

Soft corns situated as they are, deep in between two toes, show relief from pain in three to five days, and are quite permanently cured in one application with a full strength placque filtered with 0.1 mm. of brass and 1 mm. of rubber to cut out the secondary rays, and with an exposure of from forty to fifty minutes.

Several callosities of the soles have been painlessly removed without interruption of locomotion after one or two applications of such a placque for a period of one and a half hours, the lesions having been previously covered for several days with zinc oxide adhesive plaster and soaked and scraped with a dull knife to diminish their thickness and so save time.

A great many verrucous lesions have been cured in one- hour to two-hour exposures without a known failure and in thick warty lesions

extending under the edges and sides of the nails, no other known method seems to me for convenience and results, to compare with radium treatment. No damage is done to the nail bed with consequent distortion and deformity of the nail, and no trace of the lesion is left after healing has been completed.

Verruca plantaris, 7 cases, have responded after placque applications in a most satisfactory manner with a filtration of 0.1 mm. of brass and 3 mm. of rubber, applied for a duration of two hours. After three or four days the patients are able to walk with much more comfort and the only discomfort from which the patients suffer at all is at or about the twentieth day, at which time the discomfort has never been said to be even as great as it usually was before the application was made.

Leucoplakia of the mouth and leucokeratoses of the lips because of the more or less constant irritation of one kind or another to which they are subjected, are so apt to degenerate into squamous cell lesions that their presence is necessarily a matter of great anxiety to the host as well as to the physician.

Those of a syphilitic nature characterized regularly by atrophy and loss of tissue, are distinctly improved by antisyphilitic measures, and that is of course the first line of attack.

In all types of leucoplakia, smoking should be interdicted, carious and infected teeth should be removed and a most thorough oral hygiene practised. Condiments, very hot or cold and other irritating types of food, should be omitted from the diet, and besides frequent cleansing of the mouth, twice daily the parts may be dried and equal parts of lanolin and rose ointment may be applied and allowed to remain on the lesions as long as possible.

The use of caustics of any kind should be prohibited except of course the possible use of the hot cautery.

Radium, I believe, offers the most convenient and safe method of attack for such lesions that show any sign of thickening, ulceration, or a tendency to degeneration and in the purely smokers type can be usually relied upon to clear up the lesions satisfactorily. All applications should be made with the idea of producing a profound reaction. Glandular enlargements should be carefully searched for, and the patient carefully watched at monthly intervals for a considerable time after the radiation.

In the superficial smokers type, application for sixty minutes with a filtration of 0.1 mm. of brass and 1 mm. of rubber usually result in a smooth shiny eschar, and a complete disappearance of the lesion.

Where there is any tendency to induration or ulceration, at least two-hour application with 0.1 mm. of brass and 3 or 4 mm. of rubber are necessary, and where there is any suspicion of degeneration or much deep induration, in addition to such a placque 5 mg. platino-iridium radium needles are inserted all around the lesion

about a centimeter apart and diagonally directed beneath the lesion toward a central point, for two and a half to three hours. A cross-fire application is thus obtained which is most effective in clearing up such lesions.

Seborrheic or senile keratoses, occurring as they do mostly on the face and hands of older people, and particularly those who have been exposed to wind, sun and weather, demand a treatment that is effective, and at the same time leaves a good cosmetic result behind.

Radium answers these demands perhaps better than any other known type of treatment except in the very early superficial variety, that can sometimes be cleared up by a resorcin and sulphur ointment.

When the ointment does not promptly clear up these superficial lesions, a fifty- to sixty-minute application of a full strength placque filtered with 0.1 mm. of brass and 1 mm. of rubber is regularly effective, and that without a mark being left behind to show the site of the original lesion.

1a 1b

FIG. 1a.—Before treatment. Extensive, seborrheic keratoses of the face, with marked degenerations of the nose, eyelid, and outer canthus of eye.
FIG. 1b.—Same, after numerous radium applications.

Deeper seated lesions with more or less chronic inflammatory induration of their bases, or superficial ulcerations, are to be considered more or less seriously, and a ninety- to one-hundred-and twenty-minute exposure should be made after removing the crusts, resulting in a level white mark left at the site of the lesion, which tends to become more or less nearly the color of the surrounding skin as the months go by.

Very deeply infiltrated lesions or those that have apparently degenerated, should be treated as are frank epitheliomata, and

probably better by a crossfire method with 5 mg. needles inserted from beyond their edges, in beneath the lesions, directed toward a central point, plus a placque filtered as described above, and both for a duration of from two and a half to three hours.

NEVI OR BIRTHMARKS. Of the nevi the vascular types are much more responsive to radium therapy than are the cellular and pigmented lesions.

Port-wine marks are in the writer's hands more successfully treated by radium than in any other way, but, the end-results are far less proportionately perfect than in the vascular or cavernous types of lesions.

It is more effective in younger individuals, requiring a more careful technic, never to the point of real reaction. It is regularly necessary to stop short of a complete removal of the discoloration, leaving a faint pinkish color, which however is apt to disappear considerably with time.

2*a* 2*b*

FIG. 2*a*.—Before treatment. Port wine nevus on left side of face.
FIG. 2*b*.—Same, after radium treatment.

Two or, at the most, three applications are required for a given area and a third application occasionally results in the formation of large freckles that persist for many months or even years. At least three months should be allowed to intervene between applications and great care must be taken to exclude all secondary rays. Therefore a filtration of 4 or 5 mm. of rubber is necessary beside the 0.1 mm. of brass.

Fifty to seventy minutes of exposure with a full strength placque so filtered, depending on the age of the infant is as big an exposure as should be given and in the very dull red deep looking lesions more filtration with a corresponding increase in the dose is indicated. In any case a guarded prognosis should be given even though the results are sometimes really quite satisfactory.

Vascular nevi or strawberry marks, are most successfully treated by placque applications of eighty to ninety minutes with a filtration of 1 mm. of brass and 4 or 5 mm. of rubber. A faint level whitening of the skin will usually result, especially as more than one application is regularly required. Any considerable erythema is of course to be avoided.

Cavernous angiomata are also successfully treated, especially where a crossfire series of applications can be made from various areas of the circumference, directed toward the center, in order that too many rays may not have to pass through any given area of the skin overlying the lesions.

3*a* 3*b*

FIG. 3*a*.—Before treatment. Cavernous angioma, left side of face; baby, six months old.

FIG. 3*b*.—Same, after radium treatment. Two years, eleven months old.

At least 0.1 mm. of brass, 1 mm. of aluminum and 4 or 5 mm. of rubber should separate the skin or mucous membrane from the surface of the full strength placque, in order that long exposures of four to six hours can be made to get a sufficient volume of hard beta and gamma rays projected within the mass to produce an inflammatory reaction of the lining membrane of the deep-lying bloodvessels and spaces.

In lesions of the cheek, crossfire placque or tube applications from without and within the mouth can be made, remembering that the dose from the mucous membrane side should be about one-quarter less than that through the skin. Three months should be allowed to intervene between treatments. In one case under con-

stant observation a shrinkage seemed to keep up for a period of almost six months after the last radium application had been made.

Big lesions require the additional use of 5 and 10 mg. platino-iridium needles inserted around the lesions at a distance of 1 and 2 cm. from each other, but should not be left *in situ* longer than three to four hours.

Foerster[3] speaks enthusiastically of the treatment of strawberry marks and cavernous angiomata, but seems not to have obtained good results in the treatment of Port wine nevi.

Pfahler,[4] Newcomet,[5] and Robert Abbe[6] have also been successful in the treatment of these lesions with radium.

Lymphangiomata, three cases, have been successfully treated by radium placques with a filtration of 0.1 mm. of brass and 4 mm. of rubber for a duration of one hundred to one hundred and ten minutes. The lesion of the skin recurred at one edge but that responded to a second treatment including a surrounding area of skin 1 cm. beyond the lesion. The two mucous membrane lesions cleared up after two applications each for a period of eighty minutes.

Moles, pigmented nevi and pigmented hairy nevi, because of the involvement of the rete and papillary layers of the skin cannot be removed without some resulting scar. Diathermy, electrolysis, or carbon dioxide snow can accomplish their removal so much more quickly than can radium, which to be effective, would have to be pushed to massive destructive doses, that radium is certainly not the method of choice in these lesions, unless they are showing signs of degeneration.

Three cases of malignant melanomata have been treated by very big massive doses. A lesion of the forearm rapidly growing, the size of a 50-cent piece, has remained well for a period of five years. The resultant scar was excised in order that a careful microscopical search of all the scar tissue might be made, and no sign of any recurring malignancy could be demonstrated after a most careful and painstaking search. Another lesion on the forehead is well after four years, but one lesion on the toe of a woman was followed by metastatic lesions in the inguinal glands after a few months and the patient died. An amputation had been advised before radium was even considered.

Even with this inconsiderable experience with radium in such lesions but a bigger experience after extensive surgical excision, the writer would prefer to take a personal chance with radium than with surgery. Theoretically an extensive endothermy operation with the bipolar method of Wyeth, should be considered as a sane method of attack, but after all much depends on whether or not any metastatic involvement has or has not already begun. When it has, any attempt at removal in any way is of course useless. I am of the opinion that the time to attack these lesions is when they are quiescent and if possible before any metastases have occurred.

HYPERTROPHIES. Keloids and hypertrophied scars are well taken care of by radium in the form of full strength placques, and this particularly applies to young lesions that have not existed longer than six months. Old, hard fibrous lesions had probably better be excised where suitable tissue is at hand for primary suture without deformity, followed by radium exposures beginning at about the seventh day, to prevent a recurrence after excision. In these old lesions destructive doses of radium must be used if at all and although a soft pliable scar results, it does not seem to be the ideal method.

Four or five millimeters of rubber tissue should be used over 0.1 mm. of brass for a period of about ninety minutes (one-third less for very young children).

One such application frequently suffices to prevent a reformation of the keloid.

Young keloids require 2 and possibly 3 radiations at two-month intervals, with a filtration of 0.1 mm. of brass and 5 mm. of rubber, plus an added 1 mm. of aluminum, for a period of two to six hours, depending on the thickness of the lesion.

In any case, never more than the faintest erythema of the overlying skin should be produced, because of the tendency to a resulting telangiectasis.

A soft pliable, level, white skin or scar remains at the site of the lesion.

The rather severe pain that sometimes accompanies such keloidal formations, is quite regularly relieved by the first application.

Acne keloid has been reported by several authors as successfully treated by radium, but I have had no experience with these lesions except in the use of roentgen-ray.

GRANULOMAS. Granuloma annulare (two cases), cleared up quite promptly after a single radiation of seventy minutes with 0.1 mm. of brass and 2 mm. of rubber.

Pyogenic granuloma (one case) on the upper lip the size of a five cent piece, and $\frac{3}{8}$ of an inch in depth, cleared up after a single dose of three and a half hours with a filtration of 0.1 mm. of brass and 1 mm. of rubber, and with a better cosmetic result than I have ever previously obtained with either cautery or curettage and silver nitrate stick.

Granuloma fungoides, blastomycosis, and sporotricosis, should of course be as favorably influenced by radium as it is said they are at times by roentgen-ray, but the extent of these lesions has prevented any attempt on the writer's part to employ radium in their treatment.

For lupus vulgaris radium has proven to be, it is believed, one of the best means of attack in this country where we have not the Finsen light at our disposal. Two cases involving the lower half of the nose are well—1 now for eight years, and several cases around

the mouth, 2 with extensions on the mucous membrane, are healed and present only soft pliable scar tissue, with some telangiectases at the site of the skin lesions.

Small doses are entirely inadequate and placque applications corresponding to what should be 4 erythema doses, if one can speak in such terms, are necessary.

Beta rays are, therefore, the rays of choice and two- to three-hour applications are given with a filtration of 0.1 mm. of brass covered by only a few layers of rubber tissue. Successive applications frequently have to be given, and there is no advantage to be gained by a longer period between applications than six to eight weeks.

4a 4b

FIG. 4a.—Before treatment. Old, persistent lupus vulgaris, right side of face.
FIG. 4b.—Same, seven weeks after treatment with radium.

Lupus vulgaris and tuberculous ulcerations of the mucous membranes can often be healed by such a massive dose of radium, of course, with considerable discomfort to the patient. But comfort and cosmetic results are the least of one's considerations in an effort to heal lupus vulgaris lesions anywhere.

Tuberculosis verrucosa cutis lesions have also been healed in several cases, but here again big skin reactions from massive doses are necessary.

In Lupus erythematosus I cannot agree with the majority of authors that radium is ineffective in the fixed or discoid type of lesion so frequently seen on the faces of our patients. And this after a very considerable personal experience with this disease.

The disseminated type is a different proposition, portending a serious toxemia of some kind somewhere, and in patients who sur-

vive, the lesions can and do spontaneously clear up usually, without any scarring.

In the discoid type any spontaneous healing always results in scarring.

5a 5b

FIG. 5a.—Before treatment. Thick, crusted, discoid lupus erythematosus in large patches scattered over the face.

FIG. 5b.—Same, after two and three radium applications to individual lesions.

6a 6b

FIG. 6a.—Before treatment. Lupus erythematosus, fixed type, with a moderate amount of infiltration.

FIG. 6b.—Same, after treatment. One series of radium exposures.

Foerster[3] seems to have possibly explained Highman and Rulison's[7] hypothesis as to the comparative incompatibility of Lupus

erythematoses and radium therapy in the relation of pathology and effect of treatment, because of the similar end-result in both. He suggested that it may be argued that by the use of radium results are obtained analogous to those that result after the spontaneous healing of lupus, namely, atrophy and telangiectases, and that after roentgen-ray treatment, elastic tissue having been destroyed and vessels dilated, lupus lesions seem to retrogress and heal. This they actually seem to do, for no result can be hoped for short of an atrophy by the radium application.

Applications almost always have to be repeated to produce this atrophy and healing. Such repeated applications of sixty to seventy minutes filtered with 0.1 mm. of brass and a few layers of rubber tissue have healed such extensive lesions as involvement of almost the entire nose, or patches across the bridge of the nose with extensive involvements of both cheeks. Numerous large and small thick infiltrated patches on other parts of the face and head have also healed. True it is that some lesions tend to recur at the edges of the scar, but the inclusion of a considerable area of skin beyond the lesion in the radiated area has apparently resulted in a number of lesions remaining permanently well.

Skin Cancers. Krompecker, in 1900, recognized a type of cancer arising from the basal cells of the rete and in 1904 Bloodgood published an important article in which he demonstrated two important types of skin cancer, that is, the basal-cell group of Krompecker and the prickle-cell type, composed of large cells that had retained their prickles, were early destructive and grew rapidly, tended to metastasize and have a general malignancy; in contradistinction to the former group, which grew slowly, did not metastasize and were of a local malignancy only.

Degrais, a dermatologist, in 1901, treated the first case of skin cancer with radium. Since that time thousands of cases of basal-cell epitheliomata have been so successfully treated by this agent that today, I believe, there is no question but that the preponderance of opinion among surgeons who are familiar with its use is in favor of radium as the method of choice in the treatment of such lesions. This would be true for cosmetic reasons alone to say nothing of the convenience to the patient and the end-results.

In the treatment of the prickle-cell variety of lesion there is no such unanimity of opinion owing to the tendency of the draining lymph nodes to be involved, but, occasionally, brilliant results have been obtained by bold radium operators in epithelioma of the lower lip and buccal mucosa, coupled with extirpation, or irradiation of the draining lymph nodes. This has been accompanied by such good cosmetic results that it is conceivable that with an improved technic radium, alone or combined with surgery, may yet become the method of choice in this more serious type of lesion.

Cancers of the skin may be divided more or less according to their degree of susceptibility to radiation, into:

1. Basal-cell epitheliomata.
2. Lymphosarcomata.
3. Sarcomata.
4. Prickle-cell epitheliomata.
5. Nevocarcinomata (malignant mole or melanoma).
6. Epithelial carcinomata originating in sebaceous and sweat glands.

Basal-celled epitheliomata present the following more or less common clinical types as described by Hazen:[8]

(*a*) Superficial, psoriasis-like type.

(*b*) Superficial, rolled-edge type, with central ulceration or a fungus growth in center.

(*c*) Deeper ulcerating type.

(*d*) Superficial, nodular type.

(*e*) Deep, nodular type, frequently taking form of infiltrated placques.

(*f*) The morphea-like type.

(*g*) Cicatricial type, healing in center with nodules or ulcers at edge.

Usually, the location, type, character and growth serve to help us distinguish the basal-cell type but, occasionally, a really comparatively benign-looking lesion may turn out to be of the metastasizing type and one must be constantly on the lookout for a possible, rapidly developing recurrence or a beginning glandular activity. Rarely have reports come in of basal-cell tumors developing typical basal-cell metastases. One of my own cases, at the age of eighty-four years, two and a half years after removal of an apparently classical basal-celled epithelioma of the left ala of her nose developed a metastatic lesion in her left cervical region.

Fortunately, the great majority of epitheliomas of the face where a good cosmetic result is of major importance, are of the rodent ulcer or basal-cell type, with the pronounced exception of cancer of the lower lip, where absolutely the reverse holds true.

Cancers of the upper lip are usually basal-celled as are those of the lobes of the ear. Malignant lesions of the skin of the body and extremities are more frequently of the prickle-cell variety and frequently develop on tuberculous, specific or other chronic ulcers and on seborrhoic or senile keratoses, warts, moles, angiomas and nevi that are subject to more or less constant irritation, such as picking and scratching.

Leucoplakia of the buccal mucosa and lips are frequently forerunners of prickle-cell cancer in these regions.

The basal-celled type of lesion is the one that has especially interested the writer as a dermatologist and particularly those of the rodent ulcer type. These are said to occur on the face above an

imaginary line connecting the angles of the mouth with the lobes of the respective ears. Fortunately, the very great majority of skin cancers in this area are of this type, for it is here that a good cosmetic result is a matter of considerable importance, and radium gives this end-result par excellence. Particularly is this true in lesions around the eyes, of the eyelids themselves, the ears and the alæ of the nose.

Francis Carter Wood[9] estimates that the majority of human cancers require 5 erythema doses of radiation to destroy them. But, he adds, it is understood that the basal-cell tumors of the face are excepted, since it has been known for many years that most of them will disappear with 1 or 2 erythema doses, provided they have not invaded cartilage or bone, in which case a much higher dosage is necessary to be effective.

None were controlled by biopsies as lesions were on the face and cosmetic results had to be considered.

Upwards of 200 cases of skin cancer have been treated by the author since 1912. Only 10 bad results are known and, of these, 6 were cases of squamous-cell epithelioma about the face or mouth that were inoperable or had refused operations and a good result could not have been even hoped for. Of the remaining 4, 1 was an involvement of the whole lobe of the ear, 1 involved the periosteum of the right temporal bone, 1 the periosteum of the left malar bone and the fourth was an accidental leaving of a protecting sheet of lead between the eyelids and eyeball for several days with the loss of the eye. The malignant lesion had involved the periosteum as well as the inner canthus of the eye and promptly recurred. The patient lost his life under the anesthetic given for the enucleation of the eye and the removal of the periosteal lesion.

Fifteen lesions of the eyelids have been treated with good success in 14, the one failure being the case just described.

Four cases of extensive involvement of the cartilage of the ear have been treated and three of them are well with excellent cosmetic results.

Of all the cases, 13 are known to have remained well for seven years; 16 for five years and 86 for upward of three years.

Twenty-one cases have required a second application to clear up the lesion or have recurred, but healed promptly under additional applications.

The best results, undoubtedly, have been obtained in the cases treated during the past three years owing to the frequent combining of 5 mg. radium needles, inserted around or beneath the lesions with a suitably filtered placque applied to the surface. Certainly, the cosmetic results have been better, owing to the fact that this combined method required less exposure through the surface from the placque.

It may be laid down as a rule, I believe, that lesions that do not

clear up or nearly so under one single, intensive dose and certainly, after a second effort, should be promptly referred to the surgeon for surgical or endothermic removal. Such lesions probably are not of the basal-cell type or have involved the periosteum or are of that unusual basal-cell type, very rare and about which we know very little, which is exceedingly resistant to radiation.

7a 7b

FIG. 7a.—Before treatment, nodular, basal-celled epithelioma.
FIG. 7b.—Same, after radium treatment, showing cosmetic result.

8a 8b

FIG. 8a.—Basal-celled epithelioma, recurring after operation, extending into inner canthus of eye.
FIG. 8b.—Same, after radium treatment, healed four years.

A. The superficial, psoriasis-like type of lesion can be healed without scar by a full-strength placque exposure, filtered with 0.1 mm. of brass and 1 mm. of rubber for a duration of sixty minutes.

B. The Superficial, rolled-edge type, with a central ulceration or a fungating growth in the center and D, the superficial, nodular type, require a two-hour exposure with 0.1 mm. of brass and 2 mm. of rubber.

C. The deep ulcerating type and E, the deep nodular type demand the insertion of 5 mg. platino-iridium needles, inserted from beyond the circumference beneath the lesions, directed toward a central point at intervals of 0.5 to 1 cm., plus a full-strength placque filtered with 0.1 mm. of brass and 5 mm. of rubber, both for a duration of three hours or more.

9*a* 9*b*

FIG. 9*a*.—Before treatment. Ulcerating, basal-celled epithelioma of nose.
FIG. 9*b*.—Same, healed by radium, four years.

10*a* 10*b*

FIG. 10*a*.—Fungating basal celled epithelioma of temple, size of a silver dollar.
FIG. 10*b*.—Same, healed by radium, three years.

Degenerated, thick, pigmented nevi and melanomata require a similar attack but, with a duration of both for a period of from four to six hours *with* an additional 0.5 mm. of aluminum filter placed on the face of the placque.

It would seem that lesions involving the periosteum had better be treated surgically or by a combination of surgery and radiation.

Nodular lesions of the eyelids are successfully treated by the

insertion of 5 mg. radium needles placed immediately beneath them at 0.5-cm. intervals for periods of from two to four hours.

It is believed that a fertile field for bold radium operators lies in the treatment of carcinomas of the lower lip and lesions within the mouth. In these cases the coöperation of a surgeon is always essential; any glandular enlargement should demand surgical removal, and that completely, of the submaxillary and even perhaps of the cervical regions.

Two of my cases stand out so well that they will bear reporting. Both had refused operations on the lip and tongue respectively, both accepted surgical removal of glands that felt stony hard in one of their submaxillary regions and, incidentally, a careful search of the removed glandular tissue of both failed to show any malignant involvement. Both had pyorrhea and carious teeth and a dirty mouth condition. Both had been seen by several surgeons and pronounced malignant lesions.

The lip case has remained well for two years after a crossfire from the mucous membrane and skin surfaces and needles imbedded in the substance of the lip.

The tongue case was a very extensive leucoplakia with a carcinomatous degeneration of the right half, near the midline, the size of a hickory nut. This lesion healed promptly with some slight discomfort after combined needle and placque applications and has remained healed for one year. Two other small, beginning degenerations of his leucoplakia at distances of at least ½ inch from the old lesion, due to irritation from his continued excessive smoking, healed promptly after the use of needles alone.

A therapeutic test treatment of 10 salvarsan injections at three-day intervals (3.4 gm. in all) had, previous to the treatment, failed to make any appreciable effect on the lesion.

Brewer,[10] believes from statistics that he had collected "that the results of surgical treatment of lip cancers are superior to those as yet obtained by radium. On the other hand, in cancers of the cheeks the results obtained by radium are so evidently in advance of those obtained by operation that until it can be demonstrated by a series of well observed three- or five-year cases that operation will give equally good results, all cancers arising in the mucous membrane of the cheek should be treated by radium."

Broders[11] gives food for thought in lip cases when, in a resume of 537 lip cancers treated surgically, he reports a mortality of 82.6 per cent in patients with metastases and of 23.73 per cent in those in whom no metastases were demonstrated. He states that no patient with cervical lymph nodes involved or with more than one group of any lymph nodes involved had been reported living.

Lymphosarcomata should respond at least equally well to radium as to the roentgen-ray but, I have had only one experience with the latter.

Xeroderma pigmentosum (one case in a man, aged twenty-three years) has been carried comfortably and well through a period of five years, by the internal administration of arsenic at intervals and the removal of many degenerated lesions on his face, as they appeared, by radium placque applications with most excellent cosmetic results.

Five cases of roentgen-ray degeneration in old, chronic extensive roentgen-ray burns have been more successfully taken care of by radium applications and the frequent use of equal parts of lanolin and cold cream than by any other of the various methods that have been suggested.

11*a* 11*b*

FIG. 11*a*.—Before treatment. Xeroderma pigmentosum Many degenerated lesions.

FIG. 11*b*.—Same, after radium treatment.

Only exceedingly small doses of twenty-five minutes with a filtration of 0.1 mm. of brass and 1 mm. of rubber are necessary to clear up early superficial nodular or ulcerating degenerations as they arise. Larger doses are productive of long standing, sluggish ulcers that are exceedingly painful.

Cheilitis exfoliativa of both lips; two extensive cases have been cleared up after repeated, filtered placque applications.

Sarcoid of the Darrier-Roussy type; 2 cases remain well, 1 after four years and 2 typical cases of Paget's disease of the nipple, declining operation, are well after three years and one year respectively. They are, of course, under a most careful and frequent observation.

Three-hour applications with a filtration of 0.1 mm. of brass and 5 mm. of rubber are necessary in the treatment of the sarcoid lesions as these lesions are quite deeply seated in the skin.

Summary. Radium seems to stand out preëminently as the method of choice in the treatment of basal-celled epitheliomata, vascular nevi, warts of various kinds, leucoplakia of the mucous membranes, keloids and seborrheic keratoses and probably, in lupus erythematosus and lupus vulgaris.

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THE GASTRIC SECRETION: ITS BACTERICIDAL VALUE TO MAN.*

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With a Report of Bactericidal Experiments.†

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We have all been impressed, it is quite likely, by the oft repeated statement, (made in lectures, in text-books, and in writings of men interested in gastroenterology), of the so-called protective power or bactericidal power of the gastric juice. The acid secretion of the stomach, with its pepsin enzyme, is given credit for an ability to destroy swallowed living bacteria almost universally and unequivocally; and yet, if this be so, whence comes the prolific and varied bacterial flora of the gut tract? Surely not entirely by infection introduced through the anus; and more surely not even in small part can infection by way of the blood and lymph streams be given credit for the luxuriant growth of colonic bacteria. It must come by way of the stomach, from the mouth.

It has been said by Breslau in 1866, and again by Bass[1] in 1922 that within three to six hours after birth, the meconium (which

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Billroth in 1874 showed to be sterile) becomes infected, and thence onward the infant's previously sterile gastrointestinal content harbors bacteria. Whether it be for ninety hours, or ninety years, until that complex biochemical structure, his body, resolves itself into the elementary constituents of which it is composed, his gut tract remains infected constantly.

We do not know what the degree of gastric acidity is of the newborn babe. We have read, but we cannot quote the authority, however, that babies run a high gastric acidity. From personal experience in testing, fasting and digesting extractions in children from three to six months of age, of the true or pseudo-congenital hypertrophic pyloric stenotic group, we know that the free hydrochloric acid runs about as in the adult, from 10 to 40, rarely more; and that the total acid values range from 25 to 75, rarely higher, except where there is a decided stasis with the formation of excessive amounts of butyric acid. So that we think it is quite safe to assume that the function of the stomach in elaborating free hydrochloric acid and pepsin is taken up quite early in extra-uterine life.

It is probable that the infant's stomach takes on the function of elaborating gastric secretion before the first mouthful of colostrum is swallowed; and that the changing of the blood stream from the ductus venosus to and through the portal veins may have a great deal to do with the automatic starting of this secretory act. We shall welcome suggestions relative to this point. However, it may be that this function of acid and enzyme secretion is somewhat long delayed and that those organisms constituting the so-called normal flora of the bowel, entering early, begin their residence and that thenceforth, following the axiom promulgated by Noeggerath the host being "once infected remains always infected."

The history of the search for the truth as to the power of the gastric secretion to destroy living bacteria begins with, and is intimately associated with, the history of the study of the bacteriology of the feces, dating back beyond 1846.[2] Uffelman in 1881 found in the stools of infants very thin mobile rods, cocci and strepto-bacilli. Later Escherich (1886) using agar gelatin, cultured bacteria, and tried to differentiate normal saprophytic bacteria from pathogenic bacteria in the stools, and described the Bacterium coli and Bacterium lactis aërogenes. In 1899 the Bacillus bifidus communis was first described by Tissier[3] and was seen to be the commonly infecting organism in breast-fed babies. Later (1900) Moro described the acidophilus bacillus as the commonly infecting organism in the bottle-fed babies.

This, then, seems to be the first observation that the type of food could influence the intestinal flora. Evidently bacteria of certain types could survive passage through the gastric secretion of these infants. Feeding sterile food was tried by Sucksdorff (1886); by

Britzu (1895); Gilbert and Dominici (1894). These investigators found that the number of bacteria was reduced by such food. But Stern (1892), Adrian (1895), Eberle (1896), and Ballner (1904) did not find that sterile food reduced the number of bacteria.[4]

There follows a long list of investigations, from the early work of De Jager (1897), to the most recent work of Rettger and Cheplin,[5] with the one aim in view and that to change the type of the intestinal flora by feeding certain groups of bacteria—those found in buttermilk, sour milk, kefir, koumiss, matzoon and by the administration of Bacillus bulgaricus and Bacillus acidophilus. To do this it was necessary to implant these organisms in the gastric secretion. How well this has been accomplished you all know. The work of Norman[6] (1922) is along somewhat different lines, for he introduces Bacillus acidophilus from below, and combines the administration of lactose both by mouth and by rectum. A few years ago Lyon and Bartle went a step further by introducing Bacillus acidophilus directly into the duodenum by way of the duodenal tube, because they feared that many of the bacteria were being killed in their passage through the stomach.

In 1894 Cassaet[7] made some experiments with gastric juice taken from a patient having a permanent hyperchlorhydria. He allowed the secretion to remain in open test-tubes for a period of ten days, and found it still sterile at the end of that period. He then inoculated the tubes with Bacillus lactis aërogenes and Bacillus coli, but still they remained sterile. Upon neutralizing the hydrochloric acid and again implanting Bacillus coli, the tubes became cloudy within twenty-four hours and cultures yielded growths of Bacillus coli. His conclusions were as follows: (1) That the gastric juice when sufficiently acid, that is to say, corresponding to an artificial acidity of 2 per cent, is an atiseptic medium for certain species of bacteria such as Bacillus lactis aërogenes and Bacillus coli; (2) that Bacillus coli is more resistant than Bacillus lactis aërogenes; (3) that at 1 per cent, hydrochloric acid slightly retards the evolution of Bacillus coli, but that this latter brought back later into a suitable medium, rapidly recovers all its properties; (4) that it is useful to employ a 2 to 4 per cent hydrochloric acid lemonade in cases of Bacillus coli infections, as well as typhoid infections.

NOTE.—These high percentages are never attained in the human stomach, for even 100° of free acidity is only equal to 0.365 per cent HCl.

Mutch,[8] in an article published in 1914, says: "Unless the acidity is extremely diminished, only a few of the organisms can flourish. Even with marked hypo-acidity, gastric stasis is necessary for free bacterial action. The organisms which grow best in moderately acid media are Bacillus acidophilus of Moro and yeast. They can live on a medium which is acid to Congo red. Both ferment carbohydrates, the former producing lactic acid, the latter gas.

Gastric fermentation is marked when motor disability and hypoacidity occur together."

Inkster and Gloyne[9] in 1921, reported their results of experiments conducted with gastric juice from normal individuals, to test its bactericidal action on tubercle bacilli. They found that after ninety minutes exposure in a test-tube the bacteria in sputum were still viable, and that those obtained from mouth washings retained their viability after one hundred and eighty minutes exposure. From this they conclude that "the protection against the tubercle bacillus afforded by the gastric secretion is apparently by no means perfect. But it must be remembered that the dilution of the contents and the motor activity of the stomach probably play a large part in the mechanism of protection, and these latter factors cannot be satisfactorily experimented upon *in vitro*." These results are in agreement with the conclusions arrived at by Allen MacFayden[10] under different conditions and with bacteria other than Bacillus tuberculosis as long ago as 1887.

Schonbauer in 1922,[11] worked with streptococci, hydrochloric acid and pepsin. He used a 3 per cent HCl bouillon and recovered living streptococci twenty-four hours after inoculation. But 3 per cent HCl bouillon to which 2, 3, 4, or 5 per cent pepsin had been added, failed to give a viable organism after an exposure of twenty-four hours. From this experiment it seems that the bactericidal action of the gastric juice is largely dependent upon its pepsin content.

Koploff,[12] in 1923 concluded that there is no correlation between high acidity in the stomach and low bacterial numbers, or *vice versa*. Streptococci were found associated with high as often as with low gastric acidity. The fact that the bacterial count on the fasting contents is usually considerably lower than during the process of digestion, indicates that little or no multiplication of bacteria takes place when the stomach is relatively at rest; and that the greater numbers found during digestion are introduced with the food and saliva.

In this he is in disagreement with Cotton,[13] who claims that the stomach acts as a focus of infection, and through invasion of its wall by the bacteria, has its secretory function lessened or lost, thus allowing its flora to flourish unhindered. With the use of vaccines he claims to re-establish the secretion of hydrochloric acid and the elimination of the infecting organisms.

Even this short and incomplete historical resume of the literature on this subject would be incomplete without reference to the splendid paper by Knott,[14] which appeared before our work was begun, but was not reviewed until after our experiments were completed. A perusal of that paper will show how closely our results parallel those of Knott, except that he found that Bacillus coli are more resistant than the staphylococcus to the action of the gastric juice. Always, however, the question of the resistance of the particular

strain with which the investigator is working must be considered, and due allowance must be made for seemingly apparent contradictory findings. He refers to the work of Bunge[15] in 1890, who was the first to express the opinion that hydrochloric acid has an antiseptic as well as a digestant function. He also quotes Hurst[16] who studied various clinical conditions in relation to the absence of hydrochloric acid in the gastric secretion. He concludes that a constantly high level of free acidity tends to protect the individual against infection; that pepsin, combined hydrochloric acid and the organic acids play no part in affording protection.

A Review of Bacteriological Findings. There have been thousands of cultures taken of the bile of many hundreds of cases, and it was hoped at first that the result of the bacterial studies of these specimens could be analyzed, and that a complete statistical report could be prepared. But the volume of work was too great for the amount of time that could be spared at present, and we think that the same purpose will be served by taking 200 consecutive cases and giving the cultural statistics as we found them in this group. On the 200 cases there were 299 cultures made—many of these were repeated for the reason that (*a*) either the first culture was sterile, contaminated, or unsatisfactory because Bacillus coli grew so luxuriantly that it was feared that some less rapidly growing organism might have been missed; or (*b*) to check up after a period of weeks had elapsed to ascertain if a subsequent culture would give the same results as the first one.

Table I shows the result of this investigation.

TABLE I.—BACTERIOLOGICAL STATISTICS OF 299 DUODENAL CULTURES MADE ON 200 PATIENTS.

		Times.		Percentage.	Total times.
Sterile		30	=	10	
Streptococci with staphylococci		35	=	12−	
Streptococci with B. coli		27	=	9	
Streptococci with staphylococci and B. coli		12	=	4	
Staphylococci with B. coli		15	=	5	
Streptococci	Hemolytic, 30 = 10%	54	=	18	128 (Streptococci)
	Non-hemolytic, 24 = 8%				
Staphylococci	Aureus, 40 = 13%	52	=	17+	114 (Staphylococci)
	Albus, 12 = 4%				
B. coli		52	=	17+	106 (B. coli)
Pneumococci		2	=	1−	
Yeast		3	=	1	
Contamination		17	=	6+	
		299	=	100	

Giardia were found three times in 200 patients (1.5 per cent incidence).

Organisms found in bile as well as in—		Tooth socket.	Tonsil.	Tooth and tonsil.
Streptococci	Hemolytic	10	3	3
	Non-hemolytic	1	0	0
Staphylococci	Aureus	1	1	1
	Albus	1	0	0

Inasmuch as this study endeavors to answer the important question: What protection does the gastric secretion give to man against invasion of his gut tract and biliary passages by infecting organisms? —it was thought wise to study the cultural returns obtained in practising non-surgical biliary drainage as advanced by Lyon[17] in an endeavor to ascertain what effects the various motor and secretory types of stomachs would show on these cultures. At the same time an endeavor was made to reach some conclusion as to the source of the organisms found—whether it be the bile, the duodenum, the stomach secretion washing out while the drainage was in progress, the bowel below by reflux of its contents, or the tube. With these points in mind we turned to the records of 200 cases, and believed that this number should suffice if an answer were forthcoming.

The question of biliary regurgitation was investigated, hoping that some light would be cast upon the question of the normal or abnormal physiology of this act from the bacteriological aspect. It was assumed that if bile were abnormally regurgitated from the duodenum to the stomach a like process could be occurring beyond the duodenum—in the jejunum and ileum—and that perhaps Bacillus coli was being brought up from remote portions of the gut tract to be recovered in the duodenal culture. All cases, therefore, in which biliary regurgitation was noted as present or absent, either fasting or digesting in the fractional examination, or in which Bacilli coli were recovered, were gone over with this in mind. Our records were incomplete in 50, so that the analysis was based on 150 cases. Seventy-two of the 150 cases (48 per cent) showed regurgitation; and in only 28 of these 72 cases (39 per cent) was the Bacillus coli recorded as found in the duodenal culture, either alone or in company with some other organism. The other 44 cases (61 per cent) having regurgitation of bile, gave no Bacillus coli on culture.

There were, in all, 57 cases (38 per cent of the 150 cases) which gave a positive return of Bacillus coli on one or more cultures. Twenty-eight of these 57 cases showed biliary regurgitation, whereas 29 did not.

Thus, in biliary regurgitation cases there were roughly 39 per cent successful recoveries of Bacillus coli against 61 per cent failures of recovery. And in all the Bacillus coli infections of the 150 cases studied there was regurgitation of bile in, roughly, 49 per cent, and no regurgitation in 51 per cent. Can any one make a deduction, from these figures, relative to the physiology of biliary regurgitations from the bacteriological aspect? Frankly, we cannot, other than it seems that duodenal anastalsis is not necessarily an index of impaired motility in the gut tube beyond.

Again the question of stomach motility was gone into as affecting the duodenal flora, and it was found that the hypermotile cases gave

as many positive cultures as the atonic or hypomotile cases, and the sterile returns were almost equally divided between the two types.

Finally two great secretory classes were investigated:

1. The acid cases which attained at some point in the fractional analysis an arbitrary figure of 50° for free HCl, or over, as well as those which could be designated as of the continuous secretory type wherein the fasting free HCl was found over 25°, and

2. The achylia cases.

Of the former (1) there were 37 cases in 200 studied, or 18.5 per cent. The culture was sterile on one or more occasions in 13 of these 37 cases, or 35 per cent.

Of the achylia group (2) there were 15 cases in 200, or 7.5 per cent. The culture was sterile on one or more occasions in 3 of these cases, or 20 per cent.

There was no dominance of any one type of organism in the achylia cases. The cultural morphological returns ran about the same in these two great secretory classes, aside from the slight tendency toward more sterile returns in the hyperacid class.

It was hoped that a conclusion could be reached by studying those cases showing a continuous secretion. Here was a group of cases in which the gastric acidity is always high; in which the fasting residuum shows as high a free acid or a degree of acidity within a few points of being as high as the terminal high acidity found in these cases; but our hopes were ill founded. We said—if the hydrochloric acid does really protect the individual against infection, why should not a continuous type of secretion do this to a greater extent than any other type of secretion—that is, the intermittent, or so-called normal type, or the type in which the secretion is always low, or, again, the achylia type?

If we can depend upon the results of duodenal culturing in forming an opinion as to the passage of infection through the stomach and its spreading up through the bile tract, providing it be not lymph-borne or blood-borne, why should not these cases of continuous secretion fail, almost invariably, to give positive cultures; why should not these cases of continuous secretion be the ones to give us the great majority of sterile cultural efforts? We believe that the method of taking cultures from the duodenum, through a sterile tube after thoroughly washing the stomach with numerous wash waters, by which that organ is mechanically cleansed rather than chemically sterilized, and that douching the duodenum after the tip has progressed that far, is essentially a surgically clean method, and usually fails to show the ordinary organisms of contamination. Therefore we see no reason why we should not accept the bacteriological findings as correctly interpreting the presence or absence of the organisms that may or may not be infecting the host. But when we came to working out statistics to show this fact, we were

surprised to learn that there was very little difference in the bacteriological findings between the continuous secretory group and the complete achylia group. There were a few more sterile returns, it is true, but not the great preponderance of sterile returns that was expected. Besides, the low acid group and the achylia group, too, were well represented as giving sterile returns.

Here an experiment was made. Cultures were taken of the two types of bile as it was seen flowing through the tube window from patients with high acidity who were being drained by the non-surgical method of Lyon. There was to be seen, perhaps, a clear bile, but always a creamy bile passed by and was perhaps the only one observed in a highly acid case. We have shown that this creamy bile is produced by the hydrochloric acid precipitating fats and other as yet unknown substances from the bile, and possibly, too, from the pancreatic juice. However, the point is this—creamy bile means the admixture of gastric juice and bile. Now, if we try to make a culture of this bile, we shall very likely find that no growth will result, whereas the clear bile that may be found flowing an instant later, will show one or more infecting organisms. This, then, seems to be one point in favor of the gastric juice acting as a germicide—a mildly acting one it may be—but sufficiently strong to prevent the growth of the organisms in our culture medium if intimately mixed with these organisms, as they are being planted. It seems to be, as well, one point in favor of the bile being the medium carrying the infecting organisms.

The question as to what is infected—the bile, the duodenal contents, the stomach contents, or the tube—is a difficult one to answer to the satisfaction of every one. From our observations, however, we feel fairly well convinced that the bile carries the various organisms which we usually recover in the culture. We do not know that any one can definitely answer this question, but in those cases in which repeated cultures are made, the same organisms will very often be picked up time and time again. It must be remembered, however, that many patients are infected with several types of bacteria at one time, and that when the cultural reports do not agree, it does not mean that either of the bacteriological examinations is wrong. The first culture may show streptococci; the second may show staphylococci; or Bacillus coli may be the only organism recovered, even though others may be present and not found, because of the extremely rapid growth of this organism obscuring the more weakly growing bacteria. We have in mind a case which had nineteen cultures taken during the two years that he was under observation. The first culture gave Bacillus coli in pure culture. The second, taken five days later, gave Staphylococcus aureus. A third culture, two weeks later, gave Streptococcus hemolyticus and Staphylococcus aureus. There is no question in our minds that these were all there originally, but the rapidly

growing Bacillus coli obscured the others in the first culture, and it was only on the third attempt that the streptococcus, which is difficult to grow, was found. The case just referred to is of interest, too, because it showed the improvement in the cultural findings that can be brought about by the use of vaccines. The streptococci did not appear after six months' use of an autogenous vaccine. The staphylococci were more resistant; and Bacilli coli were the last to go. And we do not believe that Bacillus coli had gone forever, for we have seldom seen Bacillus coli completely removed by the use of vaccines. In this case, however, the last three cultures, taken over a period of three months, were invariably sterile.

Now let us pass on to the experiments which were made.

Experiments. The stomach content was withdrawn under the usual aseptic method which is followed in preparing a patient for biliary culture. The fluid was placed in a sterile bottle and sent to the laboratory. A time interval of from one to three hours elapsed from the hour of extraction until the experiments were started. In all 26 stomach specimens, (fasting or digesting contents and wash waters) were examined, according to the technic which follows this paragraph. Inasmuch as we were anxious to know what element of the gastric juice is responsible for its bactericidal action, it was thought wise to check our experiments with an artificial juice containing no pepsin, organic acids, acid phosphates, or combined hydrochloric acid. We would use a solution of hydrochloric acid in distilled water and see how closely it would parallel the results obtained with the natural gastric juice, at various degrees of free hydrochloric acidity. Our important question was—what effect will gastric juice of various degrees of acidity have upon those organisms commonly found in bile cultures, such as staphylococcus, streptococcus and Bacillus coli; and at what interval of time exposure will the bactericidal action be manifested? There were two other questions that we desired to answer while our investigations were being carried on. The first was—what will the bacteriological examination of these stomach extractions reveal? And, last—what effect will these gastric juices of various degrees of acidity have on Bacillus acidophilus? The tables (II, III, IV) which we have prepared from the information obtained by these experiments, give in detail the results of our efforts to answer these questions.

Technic used in Determining the Sterility and Germicidal Activity of Gastric Juice. *Bacteriological Examination.* Immediately upon receipt at the Institute, 1 cc of the gastric juice was cultured in 0.2 per cent glucose hormone broth; 2 or 3 drops were spread over a human blood hormone agar plate, and incubated for forty-eight hours at 38° C. Smears were made of the bouillon cultures and the colonies fished from the blood plates. Each microörganism isolated was subjected to the various identifying tests.

TABLE II.—BACTERICIDAL PROPERTIES OF GASTRIC JUICE ARRANGED ACCORDING TO DEGREES OF HYDROCHLORIC ACID.

Data.	Degree of Acidity.	Bactericidal Properties. Streptococci (hours).						Staphylococci (hours).						Bacillus coli (hours).						Culture.
		0	½	¾	¼	1	2	0	½	¾	¼	1	2	0	½	¾	¼	1	2	
Bile	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Staphylococcus albus.
The 8th wash water	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Bacillus subtilis.
100 cc lavage of chemical achylia	F. 0 T. 10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Bacillus subtilis, Streptococci, Bacillus coli.
Fasting content with swallowed water	F. 0 T. 10	○	○	○	○	○	○	+	+	+	+	+	+	○	○	○	○	○	○	Streptococci, Bacillus coli. Staphylococci, albus yeast.
Fasting content	F. 0 T. 10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Streptococci, Bacillus pyocyaneus, Bacillus diphtheriæ.
Fasting content	F. 0 T. 10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Bacillus subtilis, Bacillus diphtheriæ, Staphylococci albus, yeast.
Fasting content (achylia gastrica)	F. 0 T. 15	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Streptococci, Bacillus coli, Staphylococci albus, Bacillus subtilis.
Wash at end of fractional	F. 0 T. 15	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	No growth.
The 4th fasting wash	F. 5 T. 10	+	+	+	+	○	○	+	+	+	+	+	+	+	+	+	+	+	+	Staphylococci albus.
Fasting conter	F. 10 T. 25	+	○	○	○	○	○	+	+	+	+	+	+	+	○	○	○	○	○	No growth.
Fastin	F. 10 T. 25	○	○	○	○	○	○	+	+	+	+	+	+	+	+	+	+	+	+	Bacillus subtilis.

Fasting content containing saliva . .	F. 10 T. 30	+	+	○	○	○	○	+	+	+	+	+	+	+	○	○	○	○	○	Gram negative rod, thin long thread.
Fasting	F. 15 T. 35	○	○	○	○	○	○	+	+	+	+	+	+	○	○	○	○	○	○	Diphtheroid bacillus, yeast.
Fasting	F. 20 T. 40	+	○	○	○	○	○	+	+	+	+	+	+	+	+	+	+	+	+	Bacillus subtilis.
Fasting	F. 20 T. 40	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	Yeast.
Fasting	F. 25 T. 45	○	○	○	○	○	○	+	○	+	○	○	○	○	○	○	○	○	○	Bacillus subtilis.
Fasting	F. 25 T. 55	○	○	○	○	○	○	+	○	○	○	○	○	+	○	○	○	○	○	Yeast. Leptothrix.
Extraction time 150 minutes	F. 30 T. 50	○	○	○	○	○	○	+	○	○	+	○	○	○	○	○	○	○	○	Yeast, bacillus subtilis. Bacillus diphtheriæ.
Fasting	F. 40 T. 70	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	Bacillus subtilis. Staphylococci albus.
Fasting content with bile	F. 45 T. 80	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	Bacillus subtilis.
Fasting	F. 50 T. 70	○	○	○	○	○	○	+	+	+	+	+	○	○	○	○	○	○	○	Yeast.
Fasting	F. 55 T. 70	+	○	○	○	○	○	+	+	○	○	+	○	+	○	○	○	○	○	No growth.
At 135 minutes . .	F. 60 T. 85	○	○	○	○	○	○	+	○	○	○	○	○	○	○	○	○	○	○	No growth.
Fasting	F. 90 T. 105	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	No growth.
2½ hours	F. 90 T. 110	○	○	○	○	○	○	+	○	○	○	○	○	+	○	○	○	○	○	Bacillus subtilis.
1½ hours	F. 95 T. 120	○	○	○	○	○	○	+	○	○	○	○	○	○	○	○	○	○	○	Yeast. Bacillus subtilis.
85 minutes . . .	F. 100 T. 125	○	○	○	○	○	○	+	+	○	○	○	○	○	○	○	○	○	○	Bacillus subtilis.

TABLE III.—EFFECTS OF SOLUTIONS OF HCL EQUIVALENT TO THE VARIOUS DEGREES STUDIED IN GASTRIC JUICE ON BACTERIA.

Data.	Degree of Acidity.	Streptococci (hours).						Staphylococci (hours).						Bacillus coli (hours).					
		0	½	¼	⅛	1	2	0	½	¼	⅛	1	2	0	½	¼	⅛	1	2
HCl in distilled water . .																			
Representing HCl- 10 . .	10	+	○	○	○	○	○	+	+	+	+	+	+	○	○	○	○	○	○
Representing HCl- 20 . .	20	+	○	○	○	○	○	+	+	+	+	+	+	○	○	○	○	○	○
Representing HCl- 40 . .	40	+	○	○	○	○	○	+	+	+	+	+	+	○	○	○	○	○	○
Representing HCl- 50 . .	50	+	○	○	○	○	○	+	+	+	+	+	+	○	○	○	○	○	○
Representing HCl- 80 . .	80	○	○	○	○	○	○	+	+	+	○	○	○	○	○	○	○	○	○
Representing HCl-100 . .	100	○	○	○	○	○	○	+	+	+	○	○	○	○	○	○	○	○	○
Physiological salt solution control	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE IV.—EFFECTS OF GASTRIC JUICE OF VARIOUS ACIDITY ON BACILLUS ACIDOPHILUS.

		0	½	¼	⅛	1	2
Control	Physiological salt solution	+	+	+	+	+	+
23	F. 0 T. 10	+	+	+	+	+	+
24	F. 0 T. 10	+	+	+	+	+	+
26	F. 10 T. 25	+	+	+	+	+	+
22	F. 20 T. 40	+	+	+	+	+	+
25	F. 45 T. 80	+	+	+	+	+	+
20	F. 55 T. 70	+	+	+	○	○	○
21	F. 90 T. 110	+	+	+	+	+	○

Twenty-four hour growth in whey.
Arranged according to degree of HCl.
Inoculated in physiological salt solution and gastric juice of varying acidities.

Bactericidal Tests. Each gastric juice was centrifugalized at high speed immediately after culturing, and the clear supernatant fluid removed and placed in a sterile bottle. It was then placed in the refrigerator at 6° C. and held until the next morning, when the bactericidal tests were made. Subcultures of the bacteria used in the bactericidal tests were made in 0.2 per cent glucose hormone broth on the day the gastric juices were received and used the next morning in the tests. This made available for use cultures of approximately twenty hours' growth. A series of six sterile test-tubes was used for each gastric juice. In each of three tubes was placed 2 cc of gastric juice, in the remaining three tubes 2 cc of sterile physiological salt solution. To one of the three tubes containing the gastric juice was added 0.2 cc of the twenty-hour broth culture of Streptococcus viridans; to the second tube a like amount of Staphylococcus aureus; to the third tube the same amount of Bacillus coli communis culture. The three tubes each containing 2 cc of physiological salt solution were treated in a similar manner. This gave one tube containing gastric juice with one of the three microörganisms used in the tests in suspension, and one physiological salt solution suspension control of the same microörganisms. These tubes were held in a water bath at 38° C. and cultured as follows: Immediately upon addition of the bacteria to the gastric juice, one-quarter, one-half, three-quarters, one and two hours later. The physiological salt solution control was also cultured at the same time.

Method of Subculture. All subcultures of the gastric juice suspension and control were made in 0.2 per cent glucose hormone broth, with pH 7.2 which was previously tested for its cultural properties for these bacteria. Two loopfuls of a 4 mm. loop were transferred to a tube of the above medium at the stated intervals.

These subcultures were incubated at 38° C. in an incubator for forty-eight hours, when the results were read and interpreted by plus or zero signs. The plus (+) sign indicating growth. The zero (0) sign indicating no growth. The same technic and interpretations of tests were carried out in determining the germicidal properties of the gastric juice for Bacillus acidophilus, except that the culture medium used was Cohendy Whey with pH 7.6. This medium gave a most luxuriant growth of this microörganism.

The solution of hydrochloric acid equivalent to the degrees of HCl in the gastric juices tested, was prepared by adding sufficient concentrated hydrochloric acid to sterile distilled water to prepare a normal solution. Further dilutions with distilled water were made from this normal solution, and the degree determined by titration with $\frac{N}{10}$ sodium hydroxid solution. In other words a hydrochloric acid solution of 10 should be neutralized by 10 cc of $\frac{N}{10}$ sodium hydroxid solution.

TABLE V.—RELATION OF INTRAPERITONEAL AND BY MOUTH INFECTIONS IN EXPERIMENTAL ANIMALS.

Microörganism.	Method.	Nature of suspension.	Broth culture, 0.5 cc.	1 tenth cc.	1 hundredth cc.	1 thousandth cc.	1/10 thousandth cc.	1/100 thousandth cc.	1 millionth cc.	1/10 millionth cc	1/100 millionth cc.	1 billionth cc	Animals.
Pneumococcus	A	NaCl solution, 0.85 per cent	D 26 hrs.	D 22 hrs.	D 26 hrs.	D 28 hrs.	D 45 hrs.	D 45 hrs.	D 45 hrs.	D 45 hrs.	D 45 hrs.	O.K.	Mice.
Pneumococcus	B	Milk	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	Mice.
Streptococcus	A	NaCl solution, 0.85 per cent	D 22 hrs.	D 22 hrs.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	Mice.
Streptococcus	B	Milk	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	Mice.
B. anthracis	A	NaCl solution, 0.85 per cent	D 18 hrs.	D 22 hrs.	D 42 hrs.	O.K.	O.K.	O.K.	O.K.	...	...	...	Strain of B. anthracis used was of lower virulence than that used in following test, known to be of high virulence.
B. anthracis	B	Milk	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.	...	...	...	
B. anthracis	A	NaCl solution, 0.85 per cent	D 18 hrs.	D 28 hrs.	D 57 hrs.	D 74 hrs.	O.K.	D 57 hrs.	O.K.	O.K.	O.K.	...	Mice.
B. anthracis	B	Milk	D 129 hrs.	D 57 hrs.	D 57 hrs.	D 57 hrs.	O.K.	D 57 hrs.	O.K.	D 129 hrs.	O.K.	O.K.	Mice.
Streptococcus	C	NaCl solution, 0.85 per cent	D 18 hrs.	D 18 hrs.	D 18 hrs.	D 30 hrs.	O.K.	...	...	...	...	...	Rabbits.
Streptococcus	B	Broth culture, 1 cc	O.K.	...	...	...	...	...	...	...	...	...	Rabbits.

			2 billion bacteria.	1 billion bacteria.	100,000 bacteria.	1000 bacteria.	
B. tuberculosis, bovine	A	NaCl solution, 0.85 per cent	D 13 days	D 22 days	K 22 days	K 22 days	Guinea-pigs.
B. tuberculosis, bovine	B	Milk	K 22 days*	K 22 days*	K 22 days*	K 22 days*	Guinea-pigs.

* Slight tuberculosis.
A, intraperitoneally; B, by mouth; C, intravenously; D, dead; K, killed; O.K., normal.

The germicidal tests of these solutions for the three microörganisms used were almost identical with those used in the tests with the gastric juice.

What, then, should we expect of the gastric secretion in the way of killing swallowed bacteria? What is the protection it offers to the gut tract beyond? To what extent is it bactericidal? The tables we have presented give the result of many hours of patient work by Dr. Harkins in an endeavor to answer this question to our own satisfaction. In viewing these tables you should keep in mind the fact that all the organisms were naked (using an expression of Dr. Kolmer) that is—they are floating freely in a medium and are being added to gastric juice free of mucus; and are not invested by food particles or even a phagocytic cell wall. You will see that even under these ideal conditions there is a limited bactericidal value in the hydrochloric acid of the gastric juice at the normal levels of acidity. The higher the degree of acidity, the greater its bactericidal power—seems to be the rule. You will see, too, that the morphological element plays a large part in making the various organisms suceptible to the action of the acid. Again it is accepted that certain strains of the various types are more resistant than others, and many of the bacteria that are swallowed may be much more difficult to kill than those with which our experiments were conducted.

We wish here to refer to Table V. It represents the tabulated results of experiments conducted on animals to ascertain the relative resistances to a measured amount of infecting organisms, offered by the gastro-intestinal mode of administration as compared to the intravenous or intraperitoneal administration. Space does not permit of a lengthy discussion of these results, which are offered here only as a preliminary report; but a careful study of the table, using the key found below it, will show to what extent the bactericidal activity of the gastric juice was manifested.

Summary. 1. The study of the bacteriological and germicidal values was made on 26 gastric juices and wash waters of various degrees of acidity, from no free hydrochloric acid to a hydrochloric acid value of 100°.

2. Five gastric juices showed no growth, on original culture while the balance proved to contain a variety of bacteria, many of which are common to the oral cavity.

3. Practically no germicidal activity was demonstrated below a free HCl value of 10°.

4. Gastric juices containing free HCl of 10° to 20° were more germicidal for the Streptococcus viridans and Bacillus coli communis than for the Staphylococcus aureus, which organism, even in the higher degrees of acidity, has considerable resistance.

5. Gastric juice containing free HCl from 20° to 100° had a well marked bactericidal value.

6. With solutions of hydrochloric acid in distilled water the results correllated well with those obtained with the gastric juice of the same degrees of acidity.

7. Gastric juice with free hydrochloric acid between 0° and 90° had no effect on Bacillus acidophilus except in two instances; one of 55° and another of 90°. This action was only apparent after exposure for forty-five minutes or longer.

8. It is desired to impress the fact that in these exposures the organisms were naked, and not protected by food material and mucus, as they might have been under natural conditions in the stomach.

9. These results confirm, in general, those of other investigations considering the known fact that different strains of the same organism possess marked differences of resistance.

Conclusions. Thus, it can be reasonably inferred, that there is an actual bactericidal action constantly being exerted by the gastric juice because of its hydrochloric acid content (and perhaps because of some other element, chemical constituent or enzyme). Certainly a solution of inorganic hydrochloric acid is just as potent a germicide as the secreted gastric juice having the same degree of acidity. It can be inferred, also, from this study that while many bacteria are killed in transit through the stomach of a man having a normal amount of hydrochloric acid in the gastric juice, many, perhaps very many of the more resistant types, when clothed about with food particles and mucus, pass through unaffected by Nature's barrier.

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ON PANCREATIC CYSTS.

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Among the diseases of the pancreas the cysts play an important role. They are frequently recognized, either before or at operations, and by the help of surgery can usually be successfully treated. Inasmuch as cysts of the pancreas are quite rare, a report of two cases observed by me, preceded by a few data from the old and recent literature, may not be superfluous.

N. Bozeman,[1] in 1881, was the first to operate successfully upon a patient with a pancreatic cyst. The patient, a woman, aged forty-one years, had had an attack of pains seven years before in the right iliac region. Five years before the abdomen began to enlarge, slowly at first, but gradually increasing in size upon the left side. Seven months before the tumor began to grow rapidly and filled out the entire abdomen. At the same time there was considerable loss in flesh. Bozeman, Thomas and Emmet diagnosed ovarian cyst. During the operation Bozeman made the correct diagnosis. He found the uterus and ovaries normal and traced the pedicle of the cyst to the tail of the pancreas. Ten quarts of fluid were drained off by tapping, and the whole cyst removed by excision. The histology of this cyst was described by H. J. Garrigues.[2] In the discussion of Bozeman's case before the New York Pathological Society on December 14, 1881, Dr. Peabody[3] mentioned that he and Dr. Janeway had presented to the Society in January, 1879, a large cyst of the pancreas discovered at an autopsy. There was half a pailful of fluid in the peritoneal cavity containing brownish flakes. A number of calculi were found, and the walls of the cyst were made up of connective tissue lined with cylindrical epithelium, just as described by Dr. Garrigues.

Gussenbauer[4] operated upon a pancreatic cyst by attaching same to the abdominal wall and draining it. In his case the ailment was thought to have developed after overloading the stomach. The patient, aged forty years, had partaken, at a banquet, of 7 liters of stale beer and eaten 2 sausages. He was seized with abdominal pains and vomiting. The day following the patient did not feel exactly right, but could resume his usual occupation. Two weeks later, however, the patient noticed a swelling in his gastric region, which began to increase in size during the next fortnight. He lost his appetite and felt full after meals. A month later he began to vomit; lost in weight and suffered greatly from abdominal pains. Two months after the onset of the disease Gussenbauer excised and emptied the cyst; 1900 cc of a bloody fluid were emptied. The fluid

was alkaline and contained the pancreatic ferments. The patient recovered.

Wolff[5] reports 3 cases of pancreatic cysts. The diagnosis is always difficult. The examination of the stool and urine is usually negative, because in these cases there is enough healthy tissue of the pancreas left to perform all the necessary functions. In 1 case of multiple cysts of the pancreas, the cysts and two-thirds of the pancreas were excised. The patient recovered and regained normal pancreatic functions. In the second case the pancreatic cyst had assumed the size of a child's head and the walls were calcareous. Excision proved to be impossible; suture and drainage was applied. The third case was a pseudocyst, formed after a long standing necrosis of the pancreas, filling out the bursa omentalis and containing 2 liters of exudation. The bursa was opened by severing the *ligamentum gastrocolicum* and the cyst drained. All 3 patients recovered.

According to Heiberg[6] in one-third of all cases of pancreatic cyst (or pseudocysts) a trauma was the cause of the trouble. Pancreolithiasis also can lead to the formation of a cyst.

Chronic pancreatitis can likewise lead to the formation of pancreatic cysts. As an instance of this type Heiberg cites Körte's case: "A patient, aged forty-seven years, had always been well and had never suffered from any affection of the gall-bladder. On March 26 he became suddenly sick with vomiting and pains in his epigastrium. On April 10 jaundice developed, the feces being clay-colored. The extensive enlargement of the gall-bladder and the history spoke against a biliary calculus. No cachexia; no tumor palpable. On account of the severe symptoms the patient was operated upon July 2. No concrement was discovered, but the head of the pancreas was enlarged, nodulated and hard. A cholecystenterostomy was performed. The patient died on July 7. The autopsy showed hemorrhage from the sutured wound toward the inside. Pancreas enlarged, hard. The cross-section showed dilatation of the pancreatic duct. Small cyst degeneration of the head. Compression of the common duct near Vater's papilla."

A good instance of pancreatic cyst after trauma is reported by Hall.[7] Patient, aged twenty-one years, felt something tear in his abdomen when lifting a heavy load. He was sick and felt faint for a few minutes, but soon recovered and was able to work. A few days later he was seized with severe abdominal colic, requiring large doses of morphin; these attacks recurred at intervals. Five weeks after the onset of the disease the patient noticed a tumor a little to the left of the midline under the border of the ribs. The tumor gradually increased in size while the appetite failed. Patient lost in strength and weight. Shortly before the operation patient had lost 99 pounds and the tumor occupied almost the entire abdominal cavity. "With the great loss of flesh and the enormous tumor in his abdomen, the complaints of the patient of the great suffering

made a pitiable picture long to be remembered. He said that the sensation to him was that the tumor was likely to burst." The patient was operated upon by Dr. Hall and an immense pancreatic cyst was found, containing 23 pints of dark, almost chocolate-colored, thick heavy fluid, which upon analysis proved to be pancreatic fluid. Seventeen and a half days after the operation the patient died from exhaustion.

"The fact that bile regurgitated through the pancreatic duct six days after the operation demonstrated that the duct was not obstructed by a calculus; therefore we reason that if he could have been operated upon early and recovered from the operation, he might have had enough of the gland remaining to sustain life."

H. A. H. Bouman[8] reports a case of pancreatic cyst which had developed after a trauma—fall from a bicycle. The cyst was of grapefruit size and contained a bloody fluid with all the pancreatic ferments. Bouman succeeded in extirpating the cyst, and the patient made an uneventful recovery. An extensive review of the literature on pancreatic cysts can be found in Bouman's excellent article.

Regarding the non-importance of the pancreatic ferments for the diagnosis of pancreatic cyst, Opie[9] agrees with Heiberg and Lazarus.[10] Opie says: "The presence in cystic contents of one or more enzymes resembling those of the pancreas was formerly believed to give proof that a cyst had its origin in the pancreas. Not infrequently one or perhaps all of these enzymes are absent in the contents of a pancreatic cyst, whereas fat-splitting, diastatic or proteolytic, enzymes are found in fluids not derived from the pancreas."

In a number of cases of pancreatic cysts, the ferments (amylopsin, steapsin, trypsin) were found absent.

Thus Primrose[11] reports a case of pancreatic cyst which he removed six weeks after a confinement. The patient had no symptoms excepting that a large tumor filled her abdomen. This was believed to be an ovarian tumor. The operation, however, showed that there was a pancreatic cyst. Primrose succeeded in extirpating this large cyst, which he found had no connection with the ovaries but with the tail of the pancreas. In the cyst fluid all the ferments were absent. As to the relations established when the cyst enlarges, Primrose states that occasionally it comes forward between the liver and stomach; it may push the stomach immediately in front of it; it may come between the stomach and the transverse colon; it has been found between the two leaves of the transverse mesocolon; or again it may pass out below the transverse colon.

Of the newer literature we mention but a few articles. Eha[12] described a congenital pancreatic cyst in a child, aged five months. A tumor of orange size was discovered in the left hypochondrium. At operation the mass was found to be a cyst attached to the tail of the pancreas by a broad base. The cyst was dissected, the pan-

creatic portion transfixed, and the abdomen closed. The child made a rapid recovery and remained well.

The case of Bellini and Salzstein[13]—a pancreatic cyst developing after a cholecystectomy—resembles one of my own cases (A. H.). Bellini and Salzstein's case is as follows: A man, aged forty-six years, had several attacks of biliary colic. A gangrenous gall-bladder with stones were removed by operation. Two and a half, and four weeks after operation there were two attacks of colic radiating down the left anterior abdomen to the iliac region. Shortly afterward development of epigastric tumor, increasing in size and requiring operation two and a half months later. A pancreatic cyst was found containing 4 quarts of brownish fluid, with pancreatic ferments and bile. They say: "Perhaps the conclusion is justified that in cases of pancreatitis complicating gall-bladder disease, especially if there is pronounced infection, one of two methods should be followed: (*a*) cholecystostomy with drainage for several weeks; or (*b*) cholecystectomy with additional drainage of the common duct."

In some instances of pancreatic cysts the symptoms are very mild. Thus Marogna[14] reports a case of pancreatic cyst in a man, aged twenty-three years. The symptoms were a feeling of fulness in the upper abdomen, without any disturbance of digestion. The examination revealed a somewhat fluctuating tumor above the navel, extending to the left costal margin. In the urine and feces nothing abnormal was found. The operation revealed a cyst connected with the tail of the pancreas, containing 2 quarts of a brownish fluid. Drainage cured the patient in two months. Drainage seems to be the operation usually performed on account of the smaller percentage of mortality.

In some instances the course of the disease is a very protracted one and the loss of weight considerable. Bevan's[15] case is as follows: The patient, aged fifty-five years, was troubled for several years with a gradual loss of weight and a steadily increasing tumor of the abdomen. At the time of operation, the patient had lost 50 pounds in weight, while the tumor had filled almost the entire abdomen. At the operation the tumor was found to be a cyst of the pancreas containing over 2 gallons of a dark fluid with some grayish débris. Resection was impossible, so the cyst was attached to the abdominal wall and drained. Patient made a good recovery.

An excellent example of Nature's power to heal very severe, almost fatal, complications in pancreatic cysts is given by McWilliams:[16] The patient, a female, about sixty-two years of age, had been operated upon by this eminent surgeon in 1910 for a pancreatic cyst. Previous to operation the patient had been suffering from periodic attacks of pain in the left upper quadrant requiring morphin. At the time of operation there was a large transverse indistinct soft mass, not nodular, smooth, lying 4 inches below the

ensiform process. The feces contained occult blood, but no pus or red cells, or any excess of fat. A cyst, the size of a large grapefruit, was discovered at laparotomy. The needle had been inserted through the gastrohepatic omentum. After withdrawal of the needle the wall of the cyst was drawn up to the abdominal opening and a trocar and cannula were inserted, evacuating over a quart of fluid. Steapsin and trypsin ferments were found present in the fluid. A year later the patient returned with a tumor on the left side of the abdomen. An operation revealed that the cyst had filled up again. A large amount of chocolate-colored fluid was evacuated. Excision was impossible. The cavity was swabbed out with iodin solution and a drainage tube inserted. The edges of the cyst were sutured to the abdominal wound edges. For one year the patient wore the drainage tube and felt well. Then she began to complain of colicky pains. The discharge from the drainage tube increased in amount and became greenish-yellow and macerated the skin. At the same time it was noticed that food passed out from the sinus. It was assumed that the cyst wall had perforated into the duodenum. An operation was considered inadvisable. Patient got along fairly well for nine months when epigastric pains reappeared. A diagnosis of cholecystitis was made, but patient refused an operation at that time. Three months later the sinus healed completely and did not reopen afterward. About nine months later the patient was seized with agonizing colicky epigastric pain with fever, and was operated upon at the Paterson Hospital by Dr. Maclay, who removed the gall-bladder containing 54 stones. The patient has remained well ever since.

As seen from the above literature, trauma and pancreatitis form the main causes for the development of pancreatic cysts. In my own two cases which came to operation, pancreatitis was the etiological factor for the origin of the cysts.

Case Reports. Case I.—A. H., aged forty-seven years, consulted me on August 31, 1918. He gave a history of several severe attacks of biliary colic requiring hypodermics of morphin. A few days ago, after a violent attack of upper abdominal pain, principally on the right side, the patient developed jaundice. On September 4, 1918, the patient entered the Lenox Hill Hospital. He was deeply jaundiced. On palpation a resistance could be made out distinctly under the liver, which was ascribed to a filled gall-bladder. The gastric contents showed a total acidity of 70. The duodenal contents bloody; no bile; amylopsin, 1; steapsin, 0; trypsin, 0. The diagnosis was cholelithiasis with obstruction of the common duct.

September 10 the patient was operated upon by Dr. F. Torek. Several gall stones were found in the common duct and one big one was lying within and occluding the cysticus. The gall-bladder

of large size (10 cm. long), thickened and reddened, contained a watery mucous fluid without bile. A cholecystectomy was done and the patient progressed fairly well for twelve days. On September 23, however, patient was seized with violent persistent vomiting and fell into a profound collapse. Atropin was given in large doses and on September 25 the duodenal tube was introduced. The next day (September 26) the tube had reached the duodenum and ali-

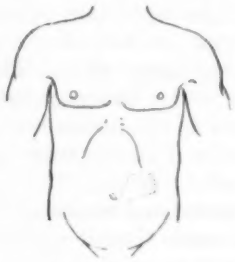

FIG. 1.—A. H., October 30, 1918.

mentation by this route was established. Patient picked up and stood the nourishment well. On October 4 the tube was withdrawn and nourishment by mouth resumed. On October 14 the patient left the hospital feeling quite well. On October 30 a mass was discovered in the left lumbar region (Fig. 1). The tumor did not appear to have any connection with the spleen, and it was questionable whether it belonged to the pancreas or left kidney. The urine was free from albumin or sugar and in this way showed that the

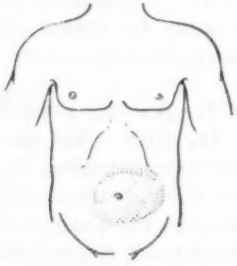

FIG. 2.—A. H., November 11, 1918.

kidneys were not markedly diseased. The patient had been treated meanwhile by another physician for a splenic tumor by application of roentgen-rays without any improvement, the tumor growing bigger all the time. On November 10, when the patient returned to the hospital, I found an extensive tumor occupying two-thirds of the abdominal cavity, starting from the left side and spreading over to the right mamillary line. (Fig. 2.) There was fluctuation

present, and a diagnosis of a probable pancreatic cyst was made. An operation was recommended. November 12 patient was operated upon by Dr. F. Torek. A big cyst connected with the pancreas was found. About 3 quarts of a dirty looking bloody fluid was aspirated out of the cyst and then drained. The fluid contained no pancreatic ferments, but there were found pus corpuscles, hematin and fatty acid crystals. The patient recovered without fever (highest temperature 100° F.) and was discharged from the hospital on December 8, 1918.

The patient presented himself on March 2, 1924, and reported that he had had no trouble after the operation, having gained about 40 to 50 pounds, and having since enjoyed perfect health.

CASE II.—B. D., married, aged forty-six years, stated that in July, 1923, he was seized with burning pains in the epigastrium. His father had died of carcinoma; his family history was otherwise negative. He consulted his family physician, who gave him tem-

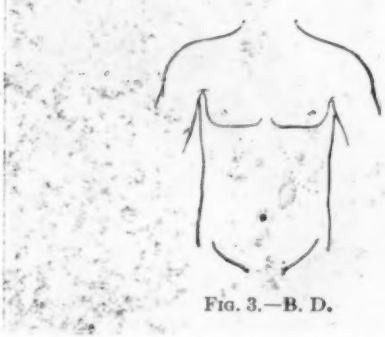

FIG. 3.—B. D.

porary relief for a while. But the patient drank heavily for about four weeks and the pains returned; but they were now located in the back of both shoulders, moving from right to left. The pains continued until August 24, when he was seized with an attack of vomiting that continued off and on for thirty hours. He had lost almost 30 pounds in weight in the last three months.

The patient came under my care on August 30, 1923. The physical findings at that time were as follows: A resistance could be felt beneath the left margin of the ribs, corresponding to the size of a fist. No nodules could be palpated, but at times fluctuation could be elicited in this area. (Fig. 3.) The tumor was situated beneath the left costal margin and was frequently visible to the eye as a bulging out body lying apparently over the stomach. At times however, the mass was not visible but could be detected by palpation. The liver was enlarged.

The roentgen-ray report (September 1, 1923), was as follows: "There is a marked defect involving the major part of the greater

curvature. (Fig. 4.) The duodenal cap is dilated and held firmly toward the liver. The cecum is filled with some irregularities at the lower pole. Stereoroentgenograms reveal a distinct pressure defect involving the distal transverse and splenic flexure.

"The above findings indicate a tumor mass causing a pressure defect on the greater curvature of the stomach. This I believe due to either a cyst of the pancreas or a tumor of the left kidney." (Dr. Priest.)

Urine: Specific gravity, 1024; albumin, 2+; leukocytes, epithelial cells, hyalin and granular casts. There was no fever on admission, and the temperature remained normal until operation.

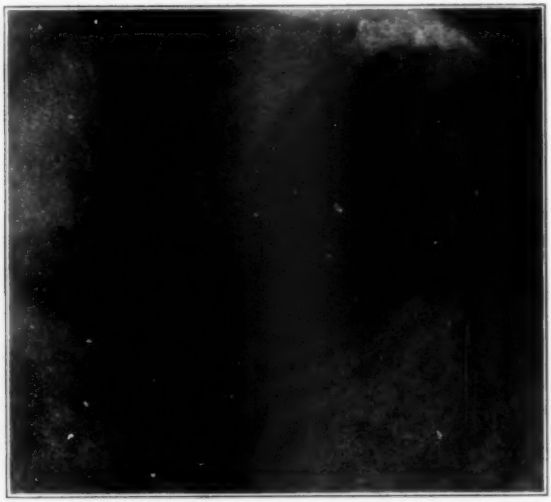

FIG. 4.—Roentgen-ray photograph of stomach of B. D. after barium. Defect seen on greater curvature, caused by pressure of the pancreatic cyst.

Duodenal contents were light greenish-yellow, turbid, alkaline (20), and contained calcium, bilirubin and cholesterin crystals and mucus. (A, 6; S, 1; T, 1.) The digestive test capsule showed remaining after seventeen hours: potato, fat; thymus (no nuclei).

Blood count: Hemoglobin, 70 per cent; erythrocytes, 5,640,000; leukocytes, 10,000, of which 5570 were polymorphonuclears and 4570 lymphocytes.

Gastric contents showed free hydrochloric acid, 46; total acidity, 60. The test for blood was negative.

A diagnosis of pancreatic tumor or cyst was made, and the patient was operated upon September 6, 1923, by Dr. H. Fischer. A pancreatic cyst was found, extending from the tail of the pancreas. The cyst was emptied, sutured to the abdominal wall and drained.

Examination of contents of cyst: Specific gravity, 1021, reaction, neutral; a trace of bile, blood test positive; urobilinogen, negative;

albumin, large amount present; protein, 3.170; sugar, 0.75 per cent (fermentation method); (A, 3; S, 0; T, 0); (cholesterin crystals, leukocytes, erythrocytes and mucus).

The patient made an even recovery and left the hospital on October 1 with a considerable gain in weight and enjoying good health.

Remarks. In the two cases just described, pancreatitis seems to have been the cause for the development of the cyst. In Case I, the patient (A. H.) had a collapse with persistent vomiting about twelve days after his operation for a calculus in the common duct, a condition favorable for pancreatic disease.

In Case II, the patient (B. D.) had a somewhat enlarged liver and used alcoholic beverages at times excessively. An alcoholic gastritis most probably gave rise to a pancreatitis which laid the foundation for the cyst.

Summary. 1. The most prominent symptoms in cases of pancreatic cysts are fulness after meals, gastric distress and vomiting at times. The larger the cyst the more distress is present.

2. The diagnosis of pancreatic cyst is not difficult, provided the cyst has assumed considerable proportions and the clinician is aware of such a possibility. The marked features which help to recognize this disease are the following:

A. There is a tumor usually in the left hypochondrium with a smooth even surface, frequently showing fluctuation.

B. The principal protrusion appears to lie in the left nipple line beneath the costal margin. The dulness produced by the mass on percussion does not extend to the spleen on the left side, nor to the liver on the right.

C. Changes in the configuration of the tumor are of frequent occurrence, dependent upon the state of the stomach (whether the latter be filled or empty).

D. There is a filling defect in the stomach due to pressure from the outside (recognizable by roentgen-rays).

E. Either a very rapid increase in the size of the tumor (within a month or two), or on the other hand a very slow protracted course (several years) is characteristic for a cyst.

3. In regard to treatment, there is only one course to pursue, and that is to operate as soon as the diagnosis is reasonably made; for without operation the condition usually leads to protracted illness, great suffering, and death. An operation, however, either removal of the cyst or aspiration and drainage after suturing the opened cyst to the abdominal wall—is ordinarily followed by a permanent cure; this occurred in the two cases described.

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THE STORY OF MAGNESIUM SULPHATE WITH SPECIAL REFERENCE TO ITS USE IN BILIARY DRAINAGE.

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Historical Review. The history of this salt presents many interesting angles. Used almost universally by physicians for many years as a purgative, it has recently had a remarkable development due largely to the brilliant work of Meltzer, who possessed the rare quality of mind that enabled him to become an eminent physiologist and a great clinician. All his contributions to physiology had a direct bearing on clinical medicine.

The town of Epsom, 15 miles from London in the county of Surrey, contained a spring which was unnoticed until about the year 1618. It is related that a farmer, named Henry Wicks, attempted to water his thirsty oxen at the spring, but to his surprise the animals would not drink. He tasted the water and found it salty and bitter. The townspeople soon began to use it as a local application in sores and skin affections. Finally Lord Dudley North had the courage to take it internally and was so greatly benefited that the water soon attained considerable fame. He published a pamphlet in 1645 entitled, "The Forest of Varieties," in which he sets forth the virtues of the water.

We are indebted to Prof. R. D. Rudolph[1] in an article in the *Canadian Medical Association Journal* for the early history of Epsom Salt. He cites the book entitled: "The Bitter Cathartic

Salt in the Epsom Water," published in the year 1695 by Dr. Nehemiah Crew, to which he had access in the library of the Royal Society of Medicine.

Epsom was soon a fashionable resort and society flocked there for the "cure." It was recommended for every known disease. Its popularity as a resort waned soon after the famous Dr. Richard Russell in the year 1753 introduced sea bathing as a remedy. The spring is still in existence but the waters are no longer used medicinally.

The use of magnesium sulphate as a purgative was soon world wide. In 1834 James Henry[2] reviewed the literature and advised the addition of dilute sulphuric acid to improve the taste. At that time the famous "Black Draught," consisting of an infusion of senna holding in suspension a mixture of magnesium and sodium sulphate was used in the hospitals and institutions. In 1866 H. R. DeRicci[3] reported the value of magnesium sulphate in the zymotic diseases, especially yellow fever. In 1900 Dr. N. F. Howard[4] in his paper entitled: "Magnesium Sulphate as a Potent Remedy," summarizes the indications for its local medicinal use as follows: (1) Scalds and burns, (2) the stings of insects, (3) bruises, contusions and lacerations, (4) joint sprains, (5) erysipelas, (6) dry salt for scalp eruptions.

Howard contrasts the opinion in regard to its use internally at that period and fifty years ago; he remarks that fifty years ago one would have been liable to suit for malpractice for using it in a case of puerperal septicemia, while in this era, failure to use it would meet with severe censure.

In 1899 F. A. Rouget[5] extolled its use in the treatment of dysentery. The use of the salt about this period may be summarized by a quotation from *Foster's*[6] *Therapeutics:*

"Magnesium sulphate or Epsom salt is a cathartic which acts promptly without giving rise to nausea or griping, produces watery stools and is rarely rejected by a sensitive stomach. It is a most useful cathartic in febrile states, colic and other conditions when a full movement of the bowels without any secondary depressing effects is desired. In the early stages of dysentery, before there are very marked changes in the intestinal mucous membrane, there is scarcely any remedy of equal value: Two-dram dose in a wine glass of water with a few drops of dilute sulphuric acid is given every hour until complete evacuation of fecal matter has taken place. The average cathartic dose is 1 ounce taken on fasting stomach."

It was largely used in acute abdominal "inflammations." I recall the lectures of the famous surgeon, Dr. E. H. Gregory in the St. Louis Medical College in 1894, who admonished his students, "For Heaven's sake do not cut a belly open without at first giving small doses of Epsom salts a trial."

In 1894 Wade[7] as well as Fincke[8] experimented in the use of the salt as a purgative by hypodermic administration. Both authors decided that it occasionally produced catharsis but was unreliable. In 1895 James H. Wood[9] concluded that the salt hypodermically produced paralysis of the inhibitory action of the nerves of the superior mesenteric plexus and thus allows free flow of liquid from the intestinal glands. The same effects are produced by large doses given by mouth.

That the drug is not without toxic effects is evidenced by the following reports in the literature: In 1891 Dr. Wm. Sang[10] in the *Lancet* reported the death of a woman who had taken 4 ounces of magnesium sulphate. He pointed to other cases and said that Taylor's work on poisons records the trial of two men in 1844 at Huntingdon who were found guilty of feloniously killing another man by administering large quantities of Epsom salts in his beer. Dr. J. Headley Neele,[11] in 1896, reported a case of poisoning in a fifteen year old boy, who had taken 2 ounces of the salt without purgation. Charles Frazier,[12] in 1909, reported in the *Lancet* 6 cases in which the administration of magnesium sulphate was followed by untoward symptoms, 5 of which terminated in death. James P. Prestley[13] reported poisonous effects following 2 teaspoonfuls of magnesium sulphate. Three weeks later the same dosage produced the same symptoms. (This was evidently a case of sensitization.) Wm. F. Boos[14] reported 10 cases of magnesium sulphate poisoning following administration of the drug by mouth. Dr. Wm. W. Anderson[15] reported 2 cases of magnesium sulphate poisoning in children with recovery. Investigation of these 2 cases showed that the children received 2 ounces of the drug, which was given in the evening, followed in the morning by a dose of thymol. One and one-half ounces of magnesium sulphate were again given at noon—an entirely unwarranted dosage.

The epoch-making work of Meltzer,[16] which appeared in 1905, was entitled: "Inhibitory and Anesthetic Properties of Magnesium Sulphate." Experiments on animals proved that intravenous injections of small doses inhibit the respiration and finally cause paralysis of the entire body. Local applications to nerve trunks block conductivity and abolish excitability of the nerves. Subcutaneous injections produce deep narcosis with complete muscular relaxation. Subarachnoidal injections produce immediate anesthesia and paralysis of the posterior extremities. All these inhibitory and anesthetic phenomena may completely disappear again. In 1906 Meltzer and Haubold[17] repeated the animal experiments on human beings with similar results. They advise the dosage of 1 cc of 25 per cent solution to 1 kilogram of body weight. The above work formed the basis for the use of magnesium sulphate in the *treatment of tetanus* forming one of the most interesting chapters in the history of medicine. Blake, in the Roosevelt Hospital,

New York, appears to be the first one to use it in the treatment of tetanus. Favorable reports soon appeared in the world's medical literature: In America by C. J. Holman,[19] George Parker[20] and others; in Germany, by Kocher,[21] Stadler,[22] Weinbrand and Unger[23] and many others, in Great Britian, by N. Markwell,[24] O. Smithson[25] and M. C. Gardner.[26] In 1916, Meltzer[18] summarized the treatment in a masterly article. The treatment of tetanus by means of magnesium sulphate is now firmly established. The subcutaneous method is growing in the favor as evidenced by recent reports of Parker (*loc cit.*) H. Stadler (*loc cit.*) and Carroll Smith.[27]

The use of the drug in surgical anesthesia was first advised by Meltzer and Auer.[28] It was used in man as an anesthetic by Chas. H. Peck and Meltzer,[29] who concluded that the employment of the salt may prove to be a practical and advantageous method, because it will produce simultaneously a moderate degree of relaxation of the muscular mechanism and because untoward effects can be rapidly reversed by the administration of a solution of calcium chloride. They believe however that it should not in the present state of our knowledge be used generally. Arthur H. Curtis[30] reports a fatal case in which magnesium sulphate was used as an aid in anesthesia and concluded that it is not safe for general use.

The fundamental work of Meltzer and the brilliant success of the salt in tetanus caused the drug to be used in a large variety of cases. Schroeder[31] reports 9 cases of chorea minor in children and 2 cases in adults rebellious to all other measures, but yielding to a 20 per cent solution of magnesium sulphate in small slowly increased doses of from 0.2 gm. to 3 gm. a day. Natali [32] as well as Cavalieri[33] reports good results in chorea. In spasmophilia good results are reported by N. Berend,[34] Genoese[35] used it in whooping-cough without effect. Hansen[36] endeavored to establish the positive action of magnesium sulphate against the toxicity of arsenic. It prolonged the average life of a series of 50 rabbits poisoned by arsenic, but cannot be said to have saved life in rabbits. It is well established as an antidote in carbolic acid poisoning. Sajous[37] states that the sulphate of sodium or magnesium should be given freely as an antidote as they form insoluble sulphocarbolates. In the event the patient survives, the sulphates should be continued for several days in small doses, inasmuch as the soluble sulphates have the quality of penetrating the tissues.

J. J. Hogan[38] treated 200 cases of influenzal pneumonia with intravenous magnesium sulphate solutions and calcium chloride solutions with mortality of 16 per cent. He strongly recommends the treatment. Weston and Howard[39] used 50 per cent solution of magnesium sulphate in 2 cc doses as a sedative, reporting very good success in 82.7 per cent of the cases. Harrar[40] reports 9 cases of puerperal streptococcemia with intravenous injections of mag-

nesium sulphate with reduction of the mortality from 93 per cent to 20 per cent.

Infected wounds are reported to be favorably benefited by treatment of magnesium sulphate solutions by Freese[41], Morrison and Tulloch[42] and others. Guggesberg[43] reports 2 cases of eclampsia without benefit. Kirkpatrick[44] used saturated solution of magnesium sulphate in corneal ulcers with satisfactory results. Meltzer[45] reaffirms the good results secured in scalds and burns, thus in an interesting manner adding the highest scientific dictum to the findings of the townspeople of Epsom.

Edward A. Leonard, Jr.,[46] reports 12 cases of delirium tremens in which lumbar puncture was done and various quantities of cerebrospinal fluid were removed according to the amount of pressure found. The amount removed varied from 10 to 40 cc. After removal of the cerebrospinal fluid, 1 cc for every 25 pounds of body weight of a 25 per cent solution of magnesium sulphate, at a temperature ranging between 95° and 100° F., was introduced by means of a syringe through the lumbar puncture needle into the canal. Ten recoveries and two deaths.

Blackfan and Mills[47] report the influence of magnesium sulphate on blood-pressure in acute nephritis. They observe that there is a lowering of blood-pressure following the administration of magnesium sulphate. When a 2 per cent solution of magnesium sulphate is given intravenously in selected cases, the blood-pressure promptly falls and remains at a low pressure for five hours. The injection is usually followed by diuresis or free catharsis.

In 1915, appeared Meltzer's[48] article on "The Relation of the Purgative Action of Magnesium Sulphate to Peristalsis and the General Law of Crossed Innervation." The experimental work of Meltzer demonstrated that solutions of magnesium sulphate produced an inhibitory influence upon the peristaltic movements of the intestinal tract of animals whether the salt was given intravenously or applied directly to the mucosa.

In 1918, Soper[49] published his article on the "Use of Magnesium Sulphate Solutions in the Treatment of Spastic Contractures of the Rectum and Sigmoid Colon." He found it to be of great value in overcoming the spastic contractures of the rectum and lower colon.

Magnesium Sulphate in Biliary Drainage. In 1917 a footnote in Meltzer's[50] article entitled: "The Disturbance of the Law of Contrary Innervation as a Pathogenetic Factor in the Diseases of the Bile Ducts and Gall Bladder," was the inspiration for Lyon's[51] brilliant work in biliary drainage. This work has not only created a tremendous amount of discussion, but has stimulated much investigation of the physiology and pathology of the gall-bladder. Lyon's five reasons for accepting the method were as follows:

1. The law of contrary innervation was correctly applicable to the biliary apparatus.

2. The color and viscosity of the bile obtained in the second aspiration (so-called "B" bile) strongly suggested that it came from its storage chamber within the gall-bladder.

3. The "B" bile from diseased gall-bladder is sometimes thick and tarry, containing mucopurulent flakes, pus cells and bacteria.

4. In cholecystectomized animals, "B" bile is not obtained by any of the aspirations.

5. In patients with gall-bladder disease treated by this method, a marked improvement has been noted.

Einhorn[52] found that the same kind of bile could be secured from patients in whom the gall-bladder had been removed. Bassler, Lucket and Lutz,[53] Dunn and Connell[54] and others also presented evidence against Lyon's conclusions. Smithies, Karkshner and Oleson,[55] on the other hand, have defended the Meltzer-Lyon method. Auster and Crohn[56] in an elaborate work on the physiology of the gall-bladder concluded that the gall-bladder is not an actively functioning organ. It does not rhythmically fill and empty itself under the stimulus of digestion. They are inclined to the belief that the flow of bile originates in the liver and sweeps down the ducts into the duodenum disregarding in main part the gall-bladder. The outflow from the gall-bladder appears to be in the nature of an overflow incontinence.

Fraser[57] in an experimental study of the use of magnesium sulphate came to the following conclusions: "The results of our experiments were entirely negative. When magnesium sulphate solution was injected directly into the duodenum of dogs or injected into the circulation there was neither acceleration of the rate of flow of bile nor change in the color. In many instances the rate was even somewhat retarded. When bile was injected into the duodenum there was a definite prompt increase in the flow of bile."

B. L. Knight[58] proposed the following theory as to the action of magnesium sulphate in non-surgical drainage of the gall-bladder. He ascribes its action to the hygroscopic quality of the drug and believes that when the congestion around the ampulla of Vater is reduced, the occluded duct opens. He gave 10 cc of saturated solution of magnesium sulphate every hour until 5 doses were given. No water or food was given for five hours, after which a dry meal was permitted. He reports very good results therapeutically.

In a recent work on the physiology of the gall-bladder, Diamond[59] supported in the main Crohn's opinion.

Personal Work. In presenting this work on biliary drainage I wish it distinctly understood that my work applies to the therapeutic use of the salt and not to its diagnostic value. Rather than detracting from the method, I believe that it simplifies the technic and will stimulate a wider use of the drug in gall-bladder conditions.

I was early favorably impressed with the therapeutic value of the method and secured many good results. Soon, however, I

noted that purgation followed the application of the salt to the duodenum and that it was impossible to withdraw more than a portion of the solution after allowing it to remain for three minutes in the gut. I observed that the feces of patients drained in this manner were colored by bile pigment. Therefore, but a portion of the bile that formed was being removed by the duodenal tube. Furthermore, I considered that inasmuch as the bile was a solution from which it was so very difficult to secure cultures, it would probably not be injurious to the intestinal tract. Moreover, it was also an important adjunct to digestion, even if contaminated by infectious elements from a diseased gall-bladder. Therefore the gut was probably a better drainage tube than the duodenal tube.

I modified the method by introducing the duodenal tube at night and giving the magnesium sulphate through it in the morning, at once removing the tube. Active purgation resulted. The stools being as a rule definitely bile colored. I continued to secure good results. One particularly severe case of Weil's disease responded well to it. I was fortunate at this time in observing a series of 12 cases of catarrhal jaundice. All the cases were fed on the same soft bland diet. The first 5 cases were treated as above outlined by means of the duodenal tube. Recovery occurred within the usual ten to twelve days' time. The remaining 7 cases were given a saturated solution of magnesium sulphate by mouth every morning on fasting stomach. The results were identical with the 5 cases in which the duodenal tube was used.

The good results secured in catarrhal jaundice emboldened me to continue its use by mouth in all sorts of gall-bladder and duct conditions. My results were as good, if not better, than they had been by the use of the duodenal tube.

The method of administration of the drug varies according to the reaction experienced by the patient. As a rule we give it in daily doses on fasting stomach for a period of one week or more. The dosage varies from ½ to 2 ounces of the saturated solution.* In some cases the continuance of small daily doses, not enough for purgative action, seems advisable. In this connection I was interested in looking over a number of case records in which old ladies attribute their freedom from further gall-bladder attacks to the habit of taking a small dose of Epsom salts every morning, a perscription that was very much in vogue during the nineteenth century.

Here I wish to emphasize that while we are enthusiastic in the treatment of gall-bladder conditions by means of magnesium sulphate solutions we do not regard it as curative. It may shorten the course of catarrhal jaundice and Weil's disease and may be of great benefit in partial inflammatory obstructions of the common

* To disguise the taste we are in the habit of adding 1 dram of compound tincture of cardamom to 1 ounce of the saturated solution. A little cracked ice may be added.

duct and in postoperative contractures of the common duct which frequently follow cholecystectomy, and in other conditions in which for one reason or other surgical operation is contraindicated or postponed. But we still entertain the conception that gall bladder disease requires surgical interference, and when such a diagnosis is established, it is the duty of the internist to advise surgery. It is a matter of common observance that gall bladder disease is subject to remissions and exacerbations, regardless of the form of treatment instituted. Therefore it is obvious that all medicinal therapy in gall-bladder disease must, in the last analysis, form *clinical impressions* rather than *concrete opinions*. We have used the method in over 300 cases and are very favorably impressed with the results.

I attempted to ascertain whether any chemical change occurred in the solution if given by mouth or by duodenal tube. The problem was submitted to the chemical department of Washington University. The following communication by Dr. A. P. Briggs answers the question: "The more I think about this problem the more I feel that there is very little which can be shown by chemical analysis. Conditions as I see them are something like this—Magnesium sulphate is certainly unchanged in passing through the stomach, unless perhaps in concentration; it may be diluted, of course, depending on the amount of fluid in the stomach, but HCl has no action on magnesium sulphate. The presence of hydrochloric acid from the stomach or of sodium bicarbonate from the pancreas may possibly have some influence on the action of magnesium sulphate in the duodenum but this cannot be determined by chemical analysis."

Magnesium sulphate given by mouth will produce the same flow of bile as when introduced directly through the duodenal tube, as may be ascertained by the following simple experiment: Pass a duodenal tube into the duodenum and give the magnesium sulphate through the tube according to Lyon's[60] technic. The following day use the same technic on the same patient (with the tube in the duodenum), except that the magnesium sulphate solution is given by mouth. The specimens of bile secured will be practically identical in both instances.

As to the action of magnesium sulphate in the intestinal tract, there has been considerable confusion and differences in opinion. Meltzer has been frequently misquoted. It appears that Meltzer did no work whatsoever on the subject of biliary drainage, but merely suggested its use. He states explicitly that sodium sulphate and magnesium sulphate are absorbed from the intestines. He produced toxic effects by injecting it directly into the lumen of the gut. On the other hand Goldschmidt and Dayton[61] in a series of elaborate experiments on animals conclude that the colon behaves toward solutions of sodium sulphate and magnesium sulphate like a semi-permeable membrane. Water is absorbed from hypotonic

solutions until iso-osmotic with the blood. With hypertonic solutions the volume increases and the concentration decreases until near the blood level. Hence there is free passage of water with no diffusion of sulphate. The failure of absorption of these salts from the colon emphasizes the specific importance of the large intestine in saline catharsis.

Wallace and Cushny[62] found that solutions of sodium and magnesium sulphate in all concentrations tend to become isotonic with the blood. The sulphates in the small intestine behave in the same manner as described in Goldschmidt and Dayton's work on the colon.

Reach[63] conducted a series of experiments on animals and found that a 25 per cent solution of magnesium sulphate applied directly to the duodenal mucosa produced an irregularly intermittent relaxation of the sphincter of the common duct, the bile being expelled in spurts. The solution applied subcutaneously and to different portions of the gut had no effect on the sphincter.

Graham and Cole's[64] recent work on roentgenological visualization of the gall-bladder is destined to throw new light on its physiology and pathology.

Meltzer always emphasized the role that magnesium sulphate played in stimulating the inhibitory phase of peristalsis. Indeed one of his first experiments showed that peristalsis stopped immediately upon direct application of the drug. He attempted to explain its action as a purgative on the theory that the salt was broken up in its passage through the stomach into sodium sulphate and magnesium carbonate, substances which he found stimulated the contractile phase of peristalsis, while the remaining unconverted magnesium sulphate stimulated the inhibitory phase. No experimental work has as yet substantiated Meltzer's theory.

I would suggest that its action might be explained on the theory of osmosis and hydrostatics, as well as the fact that magnesium sulphate produces an inhibitory effect on the *tonus* of the gut. Meltzer defines tonus as follows: "The resultant effect of the antagonistic actions may be manifest at the same place and at the same time. *This is tonus.* The degree and the character of the tonus depend upon the preponderance of one or the other factor." According to Meltzer's theory magnesium sulphate would lower the tonus, thus producing a dilatation in a given segment of the bowel, that is fugacious in character and is rapidly followed by a contraction of this dilated segment. If we can imagine that each successive segment of the bowel dilates and contracts in this manner it would explain the rush action of a dose of Epsom salts.

Summary. Magnesium sulphate is a most potent and reliable remedy and is used in a long list of diseases. Since its physiological action has been established, it is destined to have a much wider employment in medicine and surgery.

There is no essential difference in the therapeutic effect of magnesium sulphate in biliary drainage, whether it is given by mouth or applied by means of the duodenal tube. No chemical evidence exists to show that there is any difference in the solution when it reaches the duodenum, whether administered by mouth or duodenal tube. Indeed chemical opinion is to the effect that no change occurs in the solution in its passage through the stomach except possibly in concentration.*

* My thanks are due to Drs. L. E. Printy, F. R. Finnigan and L. D. Cassidy for aid in the treatment of cases. I am indebted to Dr. Finnigan and Miss Elsie Olson for help in collecting the literature.

A complete bibliography will be furnished in the author's reprints.

THE RELATION OF CHRONIC FOCI OF INFECTION TO KIDNEY INFECTION.

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The subject of pyogenic kidney infection is divided rather logically into the following parts: (1) The mode of infection; (2) the pathological anatomy of the diseased process; (3) the type of infecting organism; and (4) the source of the infection. It is the purpose of this paper to discuss primarily the source of the infecting bacteria, but such necessitates also some consideration of other parts of the subject which bear directly on this question.

There seems to be no need for a discussion of the mode of infection in acute kidney disease. The proof seems absolute that the infection is practically always of hematogenous origin. This conclusion has a most important bearing on the question of the source of the infecting organism.

The pathologic anatomy of the different types of kidney infection which we are accustomed to separate off as clinical entities is not so clearly defined. Certain types of infection have been thought by some workers to be caused characteristically by certain kinds of bacteria. Thus Cabot and Crabtree[1] associate infection by the colon bacillus with localization in the pelvic portion of the kidney, and infection by the staphylococcus and streptococcus with abscesses of the kidney cortex. This conclusion I believe to be wrong. It certainly does not agree with the results obtained by animal experimentation. In the great majority of cases it is impossible to interpret clinical pictures and laboratory findings in terms of pathological anatomy. A statement of Helmholtz is of interest in this con-

nection. He says[2] "It is clinically impossible to differentiate the different forms of kidney infection involving kidney cortex, pelvis, ureter and bladder."

Perhaps the type of infection concerning which there has been the most serious misconception is so-called "pyelitis." The symptom-complex which this term designates is very commonly met with in medical practice. A proper conception of its nature is very important from the standpoint of the origin of the infecting organism. It is probable that a true pyelitis in the sense of a simple inflammation of the lining of the kidney pelvis, rarely occurs. The clinical picture of chills, fever, pain in the kidney region and pyuria, in the absence of obstruction, is in reality usually a pyelonephritis in which the principal lesion is in the medullary portion of the kidney.

The question as to what organism is the primary invader is as yet unsettled. Cultures of the urine from cases of pyuria shows quite uniformly only the colon bacillus. This almost constant finding has confused the whole subject of acute kidney infection very materially. The presence of the colon bacillus has made it difficult for many to believe that the infection could be blood-borne. Cabot and Crabtree[3] recovered the colon bacillus from the blood in a number of cases during the chill incident to the onset of an acute kidney infection. In most of the cases studied, the infection seems to have occurred subsequent to an obstruction in the urinary tract. It is a question whether the findings were not due to direct invasion of the blood by colon bacilli already in the kidney pelvis, since Magoun[4] has shown that bacteria are capable of being absorbed through the renal pelvis and recovered from the blood stream. The finding of the colon bacillus in the blood is thus no proof of the primary casual relation of this organism to a kidney infection in which there is no obstruction.

It is well known that the colon bacillus is a ready secondary invader in the urinary tract. Le Fur[5] attempted many years ago to produce cystitis in rabbits by the injection of various organisms. He found that when the colon bacillus was injected it could be recovered in pure culture. On injecting other organisms, however, the colon bacillus was frequently recovered with the organism injected and in some instances was the only organism recovered.

Attempts to produce infection of the kidney by the intravenous injection of colon bacilli recovered from the urine of patients suffering from pyelonephritis have met with little success. Thus Helmholtz[6] found kidney lesions in only 8 of 66 rabbits so injected. The frequent recurrence of pyelitis after treatment by lavage of the kidney pelvis suggests strongly that the primary causative factor is not reached by this form of treatment.

The point should be emphasized that urine cultures are commonly made only by orthodox methods. It is quite probable that the

absence of other organisms is often thus explained. The pyogenic organisms found in areas of chronic infection often cannot be recovered by the usual cultural methods. A case of pyelonephritis which I have studied recently, is of interest in this connection. The urine contained large amounts of pus and cultures on blood-agar plates showed only a pure culture of the colon bacillus. Careful study of the stained smears of the urinary sediment showed a very few Gram positive diplococci in addition to the many Gram negative bacilli. The urine was cultured also in deep tubes of glucose brain broth. Smears from the bottom of the tube twenty-four hours later showed a few diplococci. The supernatant fluid was poured off and sterile broth added for two successive days. After the last incubation smears from the broth showed almost a pure culture of a streptococcus.

• One must conclude from the facts mentioned that there is much doubt as to the primary etiological relation of the colon bacillus to acute renal disease. There is much to suggest that the initial kidney damage is due to the streptococcus or staphylococcus. It may perhaps be continued by the colon bacillus. •

• It is probable that with infection present anywhere in the body bacteria are continually entering the blood stream and being excreted by the kidneys. The common occurrence of typhoid bacilli in the urine of patients suffering from typhoid fever is a classic example. Usually, however, the bacteria are excreted without producing evidence of kidney injury.• It is well known, however, that acute renal disease may occur during the course of an acute infection located anywhere in the body. Thus multiple cortical abscesses of the kidney are not uncommon with acute osteomyelitis.

The possible relation of chronic focal infection to kidney disease has been considered only recently. The kidney disease produced by bacteria concerned in acute osteomyelitis is due probably to the great virulence of the infecting organism. We know, however, that the organisms in chronic foci of infection are relatively avirulent. If the bacteria from such chronic foci do produce kidney disease as they pass through it must be due to some special affinity of the bacteria for kidney tissue or a selective localization in the sense of Rosenow.

To test experimentally such an hypothesis Bumpus and Meisser[7] have recently studied a series of cases of pyelonephritis to decide whether the bacteria recovered from foci of infection tend to localize in the kidney of rabbits on intravenous injection. They found that a very large percentage of the rabbits injected with bacteria recovered from chronic foci in such patients had kidney lesions while only a small number of the animals injected with bacteria from patients who were not so afflicted showed kidney localization. The organisms injected were streptococci, obtained in most instances

from dental infection. This idea that kidney infection is frequently produced by the bacteria brought to the kidney from areas of chronic infection in which an especial affinity for kidney tissue has been attained has thrown much light on the source of acute kidney infection and is reflected in different and more thorough methods of treatment. Bumpus and Meisser conclude that pyelonephritis is

FIG. 1.—Culture of a streptococcus from infected root tip in glucose-brain-broth agar. There are very few colonies at the bottom and at the top of the tube, the maximum growth being confined to the middle zone.

usually due to the streptococcus or staphylococcus with the colon bacillus as only a secondary invader. They found quite often that during the acute exacerbation following the removal of the focus streptococci as well as colon bacilli were present in the urine.

My contribution to the subject concerns primarily the study of kidney lesions developing in rabbits as a result of the intravenous injections of bacteria, usually streptococci, recovered from peri-

apical dental infection. I have also studied certain cases of pyelonephritis to determine whether the condition from which the patient suffered could be reproduced in animals with the bacteria isolated from foci of chronic infection.

The material in every case has been cultured in deep tubes of glucose brain broth and glucose brain broth agar (Fig. 1) mediums in which the organisms found in chronic foci grow very luxuriantly and also retain their elective affinity. The details of the technic employed have been described elsewhere.[8] The organisms recovered have usually been non-hemolytic streptococci. Typical organisms as seen in smears from kidney lesions are shown in Fig. 2.

FIG. 2.—Smear from abscess of kidney medulla of rabbit produced by the injection of a streptococcus from an apical abscess.

The animals have been injected intravenously with 5 cc of the twenty-four-hour brain broth culture and killed in three to six days. Four hundred and sixteen rabbits have been injected and autopsied. Of this number 166 or 40 per cent showed gross lesions of the kidney (Table I). The pathological lesions encountered have been cortical abscesses, pyelonephritis, acute hemorrhagic nephritis, and subacute parenchymatous nephritis (Fig. 3, *A–F*, Fig. 4). By far the most common type of lesion has been pyelonephritis manifested as edema, necrosis, and abscess formation in the medulla of the kidney and usually extending well down to the tip of the papilla.

TABLE I.—LOCALIZATION OF BACTERIA ISOLATED FROM INFECTED TEETH.

Number of animals	416
Percentage of animals showing lesions in:	
Joint	57.0
Kidney	40.0
Muscle	29.0
Endocardium	17.0
Myocardium	12.0
Brain	9.0
Eye	25.0
Stomach and duodenum	10.0
Gall-bladder	0.2

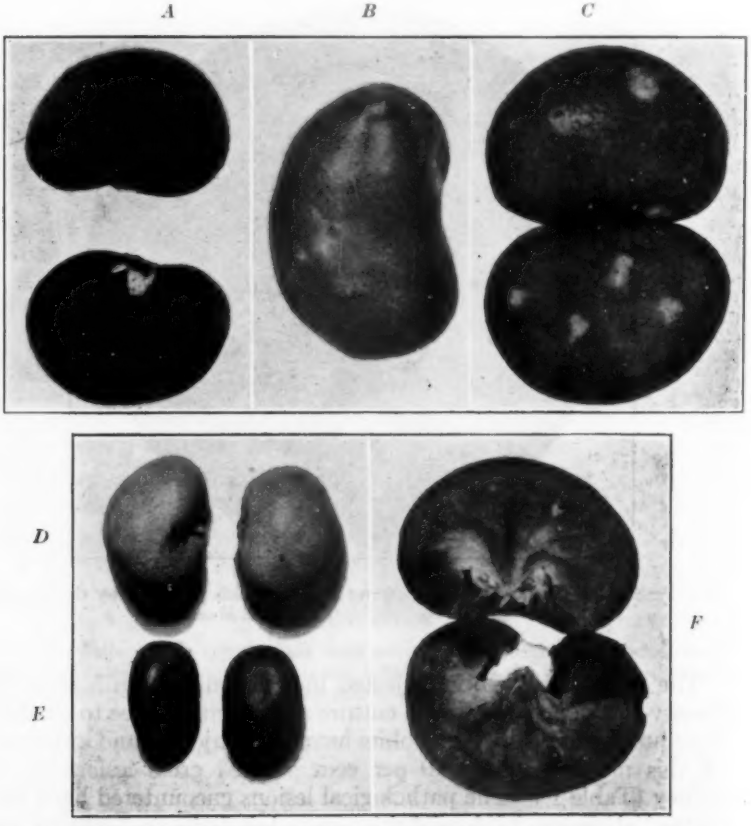

FIG. 3.—Types of lesions in rabbit's kidney produced by the intravenous injection of organisms from chronic dental foci. *A*, acute glomerular nephritis; *B*, acute glomerular nephritis and cortical abscesses; *C*, cortical abscesses; *D*, subacute parenchymatous nephritis; *E*, kidney of normal rabbit of same weight as *D*; *F*, typical lesions in kidney medulla. Note the areas of necrosis surrounded by hemorrhagic zone extending well into the tip of the papilla.

The frequency of kidney lesions occurring after intravenous injection shows clearly the great pathogenicity for kidney tissue of the bacteria recovered from chronic foci. The type of lesion produced most commonly in animals is that corresponding to the lesion occurring most frequently in patients, namely, a pyelonephritis.

Even with such evidence of the pathogenicity of the organisms from chronic foci the question remains as to what proof there is that the organism in question really causes in any particular patient the disease with which the patient presents himself. Certainly the most convincing proof we have of the relation of a focus to a disease is the reproduction in animals of the disease from which the patient

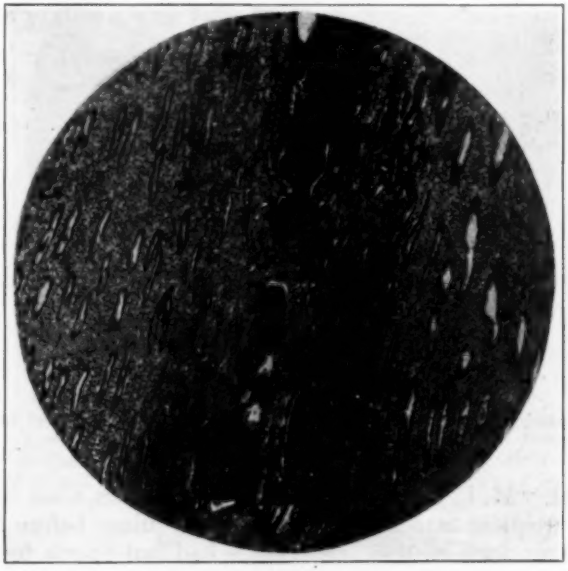

FIG. 4.—Photomicrograph through typical lesion in medulla shown in Fig. 3, *F*.

suffers with the organisms recovered from a chronic focus. Additional proof is afforded by the effect of the removal of the focus on the clinical course of the disease.

Six patients have been studied in this connection. The case histories and results of animal inoculation are given in detail below.

Case Reports. CASE I.—Mrs. J. A. P., housewife, aged forty-five years, Case No. 3702, had not felt well since a severe attack of influenza in 1918. At that time she had fever for twelve days without evident pulmonary complications. In May, 1922, she had an attack of pain in the left kidney region and a second attack in September, 1922. When first seen in October, 1922, the urine was

about one-third pus. There was a moderate amount of albumin but no casts. Stained smears of the urine sediment showed Gram negative bacilli.

The dental radiographs revealed five pulpless teeth but none showed definite rarefaction around the apex. All the pulpless teeth were extracted. Following the extraction the patient had a chill and an acute exacerbation of her symptoms. In January, 1923, lavage of the right kidney pelvis was done twice. Six rabbits were injected with the streptococci and staphylococci recovered by culture from the teeth; 2 rabbits showed no kidney lesions; 2 showed small hemorrhages in the cortex, and 2 developed multiple abscesses in the kidney medulla.

The patient has had no further symptoms and eight months after the teeth were extracted, the urine showed no pus cells or albumin.

FIG. 5.—Drawing of the kidney of rabbit injected with streptococci from apical abscesses in Case II.

CASE II.—M. I., housewife, aged forty-five years, Case No. 4524, had had frequent attacks of tonsillitis and quinsy before a tonsillectomy was done in May, 1922. She had had pyuria for twenty years and had been given pelvic lavage in 1915 without improvement. When first seen in January, 1923, she had been confined to bed for several months with myocarditis. Recently she had had an attack of acute arthritis, involving several of the larger joints.

The physical examination was negative except for an evident myocarditis. The blood count showed 4,000,000 red cells, 10,500 white cells, and the following differential: Polymorphonuclear neutrophiles, 59.6, eosinophiles, 3.2, basophiles, 0.6, lymphocytes, 32.2, and large mononuclears, 4.4 per cent. The urine contained a very large amount of pus, a moderate amount of albumin, but no red cells or casts.

The radiographs showed four pulpless teeth, only one of which had an area of apical rarefaction. The pulpless teeth were extracted. Green producing streptococci were recovered from all of them.

Four rabbits were injected with the cultures. All showed at autopsy multiple abscesses (Figs. 5 and 6) in the kidney medulla. All had purulent fluid in the joints, and five showed muscle lesions.

The patient was seen again nine months later. The heart and joint symptoms had disappeared. The urine contained only a small amount of pus. No local treatment had been given.

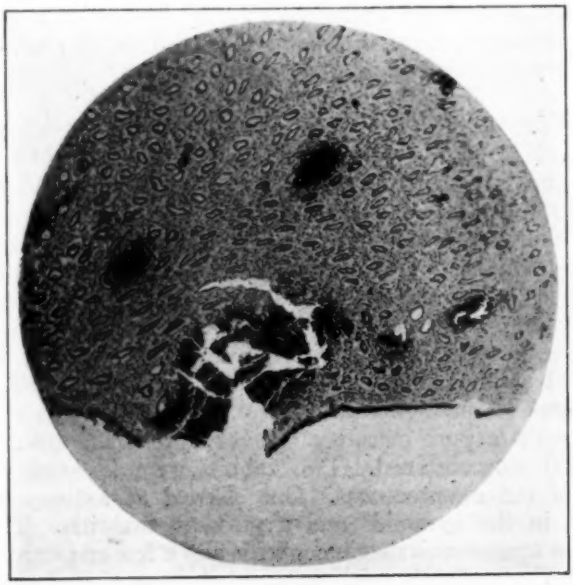

FIG. 6.—Low-power photomicrograph of portion of medulla of kidney shown in Fig. 5. Note the numerous small abscesses. One large abscess is breaking through the epithelium and discharging into the pelvis.

FIG. 7.—Roentgenograph of bicuspid tooth of Case III. The root canals are well filled, and there is no roentgenographic evidence of infection. A culture of the root tips showed a profuse growth of a short chain streptococcus.

CASE III.— C. B. P., dentist, aged thirty years, Case No. 437, had had bilateral pyelitis in 1917 which was relieved by local treatment. In January, 1922, the patient's tonsils were removed and a resection of the septum was done. In May, 1922, he had an attack of chills, fever and pyuria, followed by another in September, 1922.

The physical examination was negative except for undernutrition. The red cell count was 5,024,000 hemoglobin 100 per cent and white count 8200. The tonsils were cleanly removed.

The patient had only one pulpless tooth (Fig. 7). The roots were well filled and there was no rarefaction of bone at the root tips. A culture from the extracted tooth tip showed a large number of colonies of a green producing streptococcus (*S. salivarius*). Two rabbits were injected with this culture. One died in two hours and showed no lesions at autopsy. The other rabbit showed many small abscesses in the medulla extending down well into the papilla.

CASE IV.— W. W., a medical student, aged thirty-four years, Case No. 4274, stated that two weeks previously he had suffered from frequent burning urination, hematuria, chills and fever as high as 102° F. The symptoms improved at first under medication but the chills and fever recurred. He had had a similar attack nine years previously. There had been no other illness. The tonsils were cleanly removed. Physical examination was negative. The urine showed gross blood, many pus cells and a short chain streptococcus which was recovered by culture. One bicuspid tooth held a large inlay under which the pulp had died. There was no area of rarefaction at the tip. The tooth was extracted. From the tip a pure culture of a green producing streptococcus (*S. fecalis*) was obtained. Two rabbits were injected with the culture of the streptococcus. One showed at autopsy multiple abscesses in the pyramids and a purulent arthritis. The other showed an acute hemorrhagic nephritis and a few endocardial vegetations. The patient's urine returned to normal and there have been no further symptoms.

CASE V.— M. K., housewife, aged fifty-one years, Case No. 571, had suffered from arthritis, multiple onychia, attacks of palpitation and nycturia for many years. All these symptoms were relieved by the extraction of four abscessed teeth. Four years later the patient again presented herself because the onychia and heart palpitation had returned.

The physical examination showed marked swelling and redness around the nail root of one finger. The heart action was rapid. The sounds were distant with a tendency to gallop rhythm.

The dental radiographs showed areas of rarefaction around the roots of the lower right molar. The urine showed many pus cells and a trace of albumin. The blood count was normal. The Wassermann test was negative.

The infected tooth was extracted. The nail infection quickly subsided and the heart palpitation disappeared. A urine examination six weeks later showed no albumen or pus cells.

Cultures from the root tips showed a profuse growth of a non-

hemolytic streptococcus (*S. non-hemolyticus* 1). Eight rabbits were injected with this culture. All showed abscesses of the kidney cortex and in some there were abscesses in the medulla (Fig. 8).

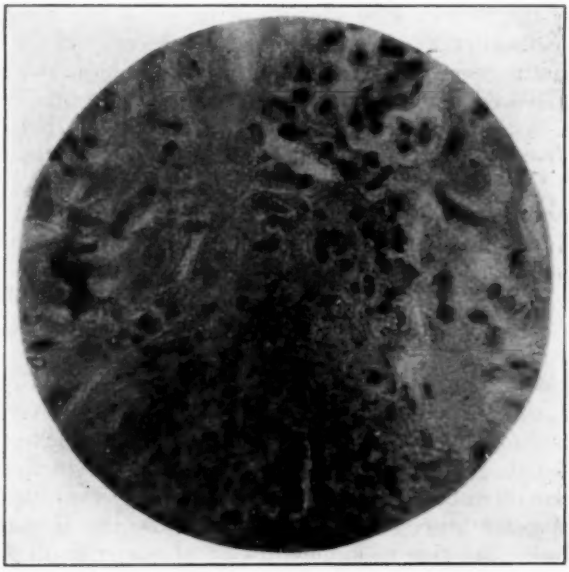

FIG. 8.—Streptococcus in medullary abscess of kidney of rabbit injected with the streptococcus from Case V (Gram stain).

CASE VI.—Mrs. L. P. E., a physician's wife, aged twenty-eight years, Case No. 7034, began to have pain in the second left lower bicuspid tooth about November 1, 1923. An inlay was removed, the root canal was treated a number of times, and a temporary filling put in. The first part of January the tooth was again painful for a week. She then suddenly began to have pain in the right kidney region. The temperature at this time was normal. The following day she had a chill, the temperature rose to 102° F., and the pain in the kidney region continued. There was some frequency of urination. The urine contained much pus and some Gram positive cocci. The fever continued for one week, the pyuria for three weeks.

Radiographs taken February 8, showed no destruction of bone or absorption from root tip of the lower second bicuspid. The peridental membrane at the tip was thickened. A root tip was present in the region of the left lower third molar. The bicuspid and the root tip were removed February 11. A profuse growth of a green producing streptococcus was obtained from both cultures.

Four rabbits were injected intravenously with 5 cc of the broth culture from the bicuspid and 2 with a like amount of the culture

from the third molar root tip. The 2 rabbits injected with the culture from the third molar showed no kidney lesions.

One of the rabbits injected with the culture from the bicuspid died soon after injection. The other 3 were killed after an interval of forty-eight hours. One showed many small hemorrhages and a few abscesses in the cortex and numerous abscesses in the medulla. The organisms were recovered by culture of the kidney. This animal also showed a few hemorrhages around the joint, and many abscesses in the myocardium. The other 2 rabbits both showed many abscesses in the medulla of the kidney with no lesions elsewhere.

Two rabbits were injected with streptococcus recovered from the kidney of one animal injected with the original culture. One showed at autopsy many abscesses in the kidney medulla with no lesions elsewhere. The other showed similar changes in the kidney and abscesses in the muscles, iritis and hemorrhages in the duodenum.

Discussion. The high incidence of kidney lesions in rabbits following the intravenous injection of bacteria recovered from chronic foci of infection demonstrates clearly that such organisms are very pathogenic for the kidney. It is an accepted fact that bacteria are often being fed into the blood stream from such chronic foci as alveolar abscesses. These facts show the importance of chronic foci in relation to kidney disease of bacterial origin.

The fact cannot be too strongly emphasized that in a patient with kidney disease of focal origin, the dental radiographs should not be relied upon to eliminate the possibility that the infection has arisen from infected teeth. This is well illustrated in Cases III, IV and VI in this series. Cultures from several hundred pulpless teeth which showed no radiographic evidence of infection, demonstrate that approximately 40 per cent harbor bacteria in sufficient number to be a possible focus of systemic disease.

Twenty-eight rabbits have been injected with the cultures from the 6 cases here reported; 24, or 89 per cent, developed gross kidney lesions. Only 40 per cent of the animals injected with bacteria from the whole group of patients (Table I) showed kidney lesions. This very much higher percentage of kidney lesions with cultures from patients who had kidney disease, shows clearly that the organisms in the infected foci here had acquired some special affinity for kidney tissue. This with the fact that the animals usually developed lesions similar to these from which the patients suffered, seems most suggestive of a causal relation of the dental infection to the kidney disease. The improvement in the patients' condition following the removal of the chronic foci makes the connection most probable.

Summary. In summary I should like to emphasize the following points:

Pyogenic kidney infection is almost always of hematogenous origin.

The pathological picture is variable and cannot be determined from the clinical symptoms.

The so-called pyelitis in the absence of obstruction is almost always a pyelonephritis.

The colon bacillus is probably seldom the primary invader except possibly in cases of lower urinary tract obstruction.

The infecting agent is usually a streptococcus or staphylococcus which produces lesions by reason, either of great virulence or an especial affinity for kidney tissue acquired in a chronic focus.

In a great majority of cases of chronic pyogenic kidney infection the organism is fed into the blood stream from chronic foci of infection.

Six cases are reported in which kidney lesions similar to those from which the patient suffered were produced in animals by the intravenous injection of organisms recovered from infected teeth.

The need for the proper consideration of chronic focal infection in treating such cases of kidney infection is apparent.

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THE MOTHER'S MILK AS A SOURCE OF INFECTION IN EPIDEMIC PEMPHIGUS NEONATORUM (IMPETIGO CONTAGIOSA BULLOSA).

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It is our intention in this paper to show that the breast milk of certain mothers may contain large numbers of Staphylococcus aureus, thus constituting a possible, albeit unrecognized source of infection for the newborn. Of the six outbreaks occurring in this hospital in three years, four seemed to originate from such milk,

a fifth was traced to an infected burn of the skin, while the origin of the sixth one was uncertain. The observations were the result of an attempt to clear up some of the interesting uncertainties regarding the mode of spread of the infection and the reasons for its persistence in institutions, once a foothold is obtained.

It is not desired to make an extensive review of the literature, which has been thoroughly covered in the review given by Foerster,[1] and also to some extent in the paper of Cole and Ruh.[2] A preliminary report by the writers has already appeared.[3]

One of the outstanding features of epidemics of this kind in institutions is their tendency to recrudesce after protracted periods of quiescence. The presumption has been that the infecting organism, namely, the Staphylococcus aureus, is particularly viable or that the hygienic conditions in the institution have been lax, or that perhaps both factors have played a part in the recurrences. On clinical grounds it has been regarded as fairly certain that the infection can be transferred from children to adults, and *vice versa* by direct contact. Certainly the view is quite reasonable, especially in light of the well-known proclivity of the organism in question for the skin.

The evidence, however, for transfer in other ways than by the direct method, together with evidence for the systemic character of the disease at times, may have a distinct bearing on the well-known persistence of the condition as well perhaps as for some of the recrudescences. We know, for example, that Della Favera[4] and Hofmann[5] have isolated the coccus from the blood stream, and the organisms are not uncommonly found in the blood of cases of Ritter's disease, which is regarded by some as simply a more malignant type of pemphigus. It appears, too, that in some cases of sepsis in the mother a pemphigoid condition of the skin may develop, as is evidenced by the studies of Staub,[6] Fehling[7] and Prissman.[8] Foerster, who quotes the work of these writers, rather regards such cases as examples of bullous exanthemata occurring in the course of septic conditions and so excludes them from the condition under discussion. Our observations suggest, however, that such segregation is of rather doubtful propriety.

As far then as the epidemiology of the question is concerned, it may be stated that, although it is not difficult to account for transmission during an epidemic, once it is started, it is often particularly difficult to find the source of the infection as well as to account always for the recrudescences.

For this reason we have been especially concerned in studying carefully the *initial* cases of each outbreak which has followed a period of quiescence. Our attention in such cases has been focused on the mother also, on account of the evidence from our first case suggesting that through her milk she was a carrier of the infection.

Bacteriology of Mother's Milk in a Sporadic Case of Pemphigus Neonatorum. The lesions of the baby were first noticed

on the thighs, appearing on the eighth day after birth. Three days later the face and head were involved. The lesions began as typical blisters, most of which later developed to the pustular stage. Following rupture of the vesicles a marked desquamation took place over areas several centimeters in diameter, leaving a moist reddened substratum. The lesions on the face and head developed about the same time that the baby was taken off the mother's milk. They disappeared within a few days.

As soon as the lesions were discovered on the baby attention was directed to the mother. It was learned that about the fifth day following delivery she developed a mildly erythematous type of itching rash, which appeared first on the arms about the elbows and was quickly followed by the same type of lesion on the legs and on some other portions of the body. At no time did any rash develop on the face. With the exception of the skin of one breast, where a few of the most minute whiteheads or pustules later developed, nothing resembling impetigo was present on the mother's skin. The rash itself occurring in an obstetric patient was not such as to excite any special attention, and resembled nothing so much as an ordinary drug rash. Over the shoulders it took on a macular appearance and on the arms and legs was more of a diffuse erythema. In three or four days it was gone.

For reasons which will appear later on, in connection with the first case that occurred in this institution a culture of the milk was made first under aseptic conditions. The nipple and areola were first thoroughly washed with green soap and then with bichloride, which was followed with boric acid. With a sterile breast pump 5 cc of milk was withdrawn and immediately cultured on a blood-agar plate with a 3-mm. platinum loop. Approximately one hundred colonies of pure Staphylococcus aureus and albus developed. The colonies were surrounded with a broad zone of hemolysis and those of the aureus greatly outnumbered the albus. At this time one or two of the most minute pimples were observed on the breast, and culture of these yielded the same organism. No cracks in the nipple were apparent.

The question then arose regarding the origin of the organisms within the breast. Did they come from the blood or were they introduced from the skin? Perhaps this question can never be answered with finality, yet the evidence rather points to the former alternative. We also wished to know whether the organisms were growing in the ducts of the nipples alone, or if they were generally disseminated throughout the glands. To obtain some idea of this we first obtained about 5 cc of milk from both breasts—fractions *A* and *B;* these were put into sterile containers and then practically all of the remainder of the milk withdrawn from the breasts and discarded. With fresh sterile pumps the residual fractions—*C* and *D*—were withdrawn. Assuming that we had by now thoroughly washed out the peripheral ducts, the residual frac-

tions were held to be derived from the deeper recesses of the breasts. The four fractions were streaked on separate quadrants of the same blood-agar plate, and they showed approximately equal numbers of the organism in almost pure culture. In spite of the abundance of organisms present, and their apparent wide dessemination throughout both breasts, no evidence of mastitis was found either clinically or from microscopical examination of the centrifuged sediment. Cultures of the blood, throat, stool and cervix were negative for the specific organism. In fact, a culture of the cervix grew no organism, so it was highly improbable that the vaginal tract was the portal of entry. The catheterized specimen of the urine, however, showed a few colonies of the organism. These findings, together with the rash which occurred rather generally over the body within a short space of time, suggest that the infection, mild though it was, was systemic in character.

Specific inquiry regarding the possible source of infection failed to reveal any very positive evidence. The patient did say that a sweater borrowed from a family in which there were several children was worn by her for a few days following delivery, after which she noticed an irritation on her arms to such an extent that the sweater was removed. Simultaneously the rash appeared on her neck. It could not be established that the children in the house from which the sweater was obtained had infection of any sort, and its connection with the development of the rash may have been pure coincidence. However, it is very much to the point that at the time of entrance of the woman to the hospital numerous cases of this disease were present in the community, so it would seem probable that she brought the infection with her, perhaps as a carrier. Careful segregation of both mother and infant prevented further cases of the condition in the hospital. To our knowledge at least one case of Ritter's disease existed in the community at this time.

We then directed our attention to the probable route of infection in the baby. Inasmuch as the milk was so heavily infected, it was logical to believe that the organisms might have passed through the intestinal canal, and their elimination in the feces have been responsible for the initial lesions that occurred on the thighs of the infant. This theory of the mechanism of infection was made decidedly improbable when a culture of the stools of the infant was found negative as far as the Staphylococcus aureus hemolyticus was concerned. Furthermore, had the infection been presumed to have arisen by direct contact, one would have expected it to occur first about the face of the infant, because while nursing it made daily contacts with the skin of the mother's breast, the minute pustules of which were proven to contain the infective organism. The fact that the infection of the face and head did not occur until several days after the appearance of the lesions on the thighs was rather against the theory of direct contact. As soon as the baby

was taken away from the mother's milk it immediately began to improve, and the lesions of the face cleared up completely in less than forty-eight hours, and as was to be expected the baby made an uneventful recovery.

If we are to assume that the organisms ingested by the infant in the milk produced a systemic infection, if would seem that they must have invaded the intact mucosa of either the upper respiratory or the gastrointestinal tracts. In confirmation of this point, we were already in possession of the following experimental evidence which we had obtained about a year previously. Freshly isolated cultures of some the more severe cases of the epidemic of this condition, which began in January, 1922, were fed to young guinea-pigs in milk (Table I).

TABLE I.—PROTOCOL OF FEEDING EXPERIMENTS.

Feeding-date, 1922.	Guinea-pig No.	Age of pig.	Feeding duration.	Result.	Culture.
Feb. 9	385	3 days	4 days	Died, Feb. 12, 1922; massive pneumonia in both lungs	Heart blood negative Staphylococcus aureus in purity from lung.
Feb. 9	386	3 days	4 days	Died, Feb. 13, 1922; massive pneumonia in both lungs	Staphylococcus aureus from both lungs in purity.
Feb. 10	387	4 days	15 days*	Died Mar. 2, 1922; abscess; sepsis; no pneumonia	Staphylococcus aureus in heart's blood.
Feb. 14	388	Full grown	10 days	Negative; died, Feb. 24, 1922, of guinea-pig pneumonia	Mixed infection apparent from smears of bronchi; no growth on Difco agar.
Feb. 14	389	Full grown	10 days	Negative; died Apr. 28, 1922, of typical guinea-pig bronchopneumonia	No cultures.
Feb. 17	392	17 days	7 days	Negative; died Apr. 28, 1922 of guinea-pig pneumonia	No cultures.
Feb. 20	393†	Full grown‡	Not fed	Died, Feb. 20, 1922, 11 days after first feeding of offspring	Pure culture staphylococcus from lung.
Dec. 23	493	9 days	13 days	Negative; strain is now about a year old	
Dec. 23	494	9 days	13 days	Negative; strain is now about a year old	

* Then inoculated 5 cc subcutaneously.

† Presumably contracted the infection from a nursing pig, inasmuch as it gave suck to Nos. 385, 386 and 387. Nos. 385, 386 and 387 received cultures freshly isolated from cases of pemphigus neonatorum. No. 388 received a culture derived from the lungs of No. 385. Nos. 389 and 392 received cultures from the lungs of No. 386. Nos. 493 and 494 received fresh cultures of the same strain as No. 385.

‡ Mother of Nos. 385, 386 and 387.

TABLE II.—FRESHLY ISOLATED CULTURES FROM MILK OF WOMAN DESCRIBED IN TEXT.

Feeding-date, 1923.	Guinea-pig No.	Age of pig.	Feeding duration.	Result.
May 2	523	9 days	15 days	Negative.
May 2	524	11 days	14 days	Negative.
May 2	525	3 days	2 days	Pig died, but so mutilated by his fellow pigs that no autopsy was possible.
May 2	526	1 day	12 days	Negative.
May 2	527	1 day	12 days	Negative.

Animals Nos. 385 to 393 inclusive and Nos. 493 and 494 were fed morning and evening with 1 cc of 0.9 NaCl suspension of the organisms, about 5,000,000,000 to 1 cc. A medicine dropper was used. Pigs Nos. 523 to 527 were fed in the same way, but milk was used as a menstruum instead of NaCl.

Of the 3 pigs first treated, ranging in age from three to four days, 2 died in less than a week, and much to our surprise the lesions found at autopsy were those of diffuse double pneumonia. From these lungs the staphylococci, which could be seen in large numbers, were readily isolated. One of the adult pigs that suckled the young ones while the latter were being fed the infected milk in some unknown way contracted the pneumonia, and from the lungs of this pig also were recovered the staphylococcus in purity. Three grown pigs fed for ten days showed no immediate effects, but in two months died of typical guinea-pig pneumonia. The young pigs died after four days' feeding. It should be stated that when pigs Nos. 385, 386 and 387 died we were not having other pigs die of spontaneous pneumonia. Pigs Nos. 388, 389 and 392 succumbed to this disease at a somewhat later period.

It would seem, therefore, that these organisms passed through the intact mucosa of these animals and were filtered out by the lungs, where in some cases their presence set up an active inflammatory condition resulting fatally. Whether the organisms were absorbed from the upper part of the respiratory tract and passed down the tracheal lymphatics, as is now regarded by some as a pathway for the development of pneumonia, or whether they were absorbed from some part of the gastrointestinal tract, cannot be stated.

The whole equestion of the passage of organisms through the intact mucosa of the gastrointestinal and respiratory tracts is one of great interest and considerable work has been done on the subject. Usually, however, avirulent organisms easily recognized culturally have been employed, as was the case with the work of Williamson and Brown,[9] in the Mayo Clinic, with Bacillus prodigiosus. Many of these experimental results have been negative,

and it would seem that the virulence of the organism would be of first importance in such work, especially if we regard virulence as the capacity of the organism to multiply in the tissues. In support of our opinion in respect to the relation of the virulence of organisms to their passage through the intact mucosa, we quote the work of Thiele and Embleton,[10] who were unable to demonstrate the presence of Bacillus mycoides, Bacillus coli and Bacillus prodigiosus in the blood stream after feeding, while anthrax bacilli were found in the lungs and urine four hours after feeding.

In the same connection it was of considerable interest that the cultures which gave us positive animal results soon after isolation were completely negative when tried on young guinea-pigs about a year later, after the cultures had been kept on artificial media (Table I, pigs Nos. 493 and 494). It was of interest, too, that we failed to repeat the results with fresh cultures of the organism from the case just described (Table II). Therefore we are inclined to draw the conclusion that the organism was of slight virulence, as indeed was to be suspected from the mild character of the reaction both in the mother and in the child. The cases were by no means as alarming clinically as the earlier ones.

Results of Subsequent Outbreaks. No further cases of the disease occurred until August, 1922, when another single case occurred with findings very similar to the one studied, except there were not nearly so many organisms in the mother's milk. However, they were pure Staphylococcus aureus, while the milk of other mothers cultured at this time were either negative or showed an occasional colony of Staphylococcus albus.

An outbreak of 10 cases occurring in October, 1923, gave opportunity to study the milk of numerous mothers, both those having infected babies and those with normal babies. This was especially desirable if we were to verify our suspicion that single cases, such as have been described, might form starting-points for other cases. It was of interest, then, that here again we found that the mother's milk of the first baby to come down contained pure Staphylococcus aureus in considerable numbers. This was also true of the mother's milk in one other case in this outbreak. All other mothers or cases were either negative or had a few colonies of albus. In addition the milk of six mothers with normal babies showed the same negative findings. The cocci were identified culturally, chiefly by pigment production and reaction to mannite, and serologically by the agglutination reaction. One other small outbreak showed similar findings.

Perhaps the most striking instance of all was the latest outbreak, July, 1924, which involved not only the mother's own baby (Baby Z), but also a seven months' premature infant (Baby V) fed with the same milk, because the premature's mother had practically no milk. Baby V, the premature, was born two days after Baby Z,

and on the same day both babies developed the skin lesions of pemphigus, Baby V having a few scattered pustules and Baby Z having one large vesicle on the back of the neck. From the lesions of both babies Staphylococcus aureus with a few albus were found in abundance. It is of note that clinically the premature did not tolerate the milk of the Z mother, as was evidenced by a rapid rise of temperature with gastrointestinal symptoms. These results in Baby V recall the feeding experiments with young guinea-pigs. After thirty-six hours it was given artificial feeding. No further lesions developed.

Except for the above sequence of events there would have been no reason to have suspicioned the mother, who was in splendid health and possessed an abundance of milk. Nevertheless, her milk obtained under rigid aseptic precautions yielded about twenty-five colonies of Staphylococcus aureus and a few Staphylococcus albus from our 2-mm. platinum loop seeding of an uncentrifuged sample. She had no lesion of any sort about the nipple or skin of the breast.

For control purposes it is of interest in this connection that a woman who had a small Staphylococcus aureus abscess in the subcutaneous tissue near the nipple yielded a milk with no Staphylococcus aureus. Her baby, too, was normal. This small outbreak above referred to occurred following a quiescent period of more than two months. The isolation precautions taken with both mother and children have prevented any new cases, which has been repeatedly shown in our experience to justify the procedure. It appears that early recognition of even mild cases and their rigid segregation, together with the mother whose milk contains the organisms, is of primary importance in preventing spread of a disease *that at intervals is being introduced anew into the institution.*

The results that may follow in the wake of unrecognized infection of Staphylococcus aureus, regardless of their source, is illustrated by the following outbreak originating apparently from a burn. It resulted in 6 cases, which in a week or so were followed by at least 12 more.

Outbreak Traceable to a Skin Infection from a Burn. This small series of 6 cases occurred in February, 1924, the initial case being a baby on whose chest a mild burn developed, caused by a mustard plaster. The infection was pure aureus, and then quickly followed 5 other cases, apparently contact infections. The mother's milk in the initial case was negative, however, as was to be expected, indicating that the origin of two such outbreaks might be quite different.

Search for the Epidemiological Type of Staphylococcus Aureus. The outbreak following the burn case indicates that Staphylococcus aureus from pathological processes other than pemphigus may give rise to the disease, in which event we would

not expect to find by serological methods an epidemiological type of infecting aureus. This latter consideration was entirely borne out by study of many strains of Staphylococcus aureus of diverse origin which we have collected in the past three years. The detailed study will be reported separately. In this connection it is pertinent that covering a period roughly coinciding with that of the pemphigus outbreaks we have frequently isolated Staphylococcus aureus from lesions in almost every part of the body. This fact testifies for the systemic transfer of these cocci but without active sepsis, and makes it entirely conceivable that in the breast milk of the mother suffering from the rash, the origin of the cocci may have been hematogenous.

Discussion. Infection by way of the milk was suggested to us by the first case of the disease that was brought into the institution in the first week in January, 1922. The significance of the findings was not apprehended at the time, partly because the condition was not even known to be epidemic in the locality and partly because the mother was mildly septic. In this instance the mother developed a rather severe sore throat on the day of delivery, from which a staphylococcus was isolated from among the other organisms present. She also developed a septic type of temperature which ran for several weeks and a staphylococcus was isolated from her blood stream early in the course of the infection. About the fifth day a slight itching rash appeared, distributed irregularly over the body, but no lesions were discovered on the breasts. The rash was not as marked as in the 1923 case, and there was no evidence of pustule or vesicle formation. Like the other rash, it was rather evanescent in character.

Following the appearance of the coccus in the blood on the third day after delivery the lesions of typical pemphigus appeared on the baby on the ninth day, or four days after the rash first showed on the mother. This case did not come to our attention until other cases began to appear, and it could not be ascertained with certainty whether the latter originated from the mother or child of the first case, or whether they were of independent origin. The cultures of the child were of the same Staphylococcus aureus hemolyticus, as indeed were all the subsequent cases cultured, which numbered approximately two dozen. Before we became aware of the significance of the situation the mother with the blood infection left the hospital, and it was not possible to study her further. Although no cultures were made of the milk, it was surmised that infection in the baby might have occurred through it, since the coccus was present in the blood and since there were no other lesions apparent whereby the child could have gotten its infection from the mother. It seems reasonable to assume that for the past two years hemolytic staphylococcus infections have been epidemic, which is entirely comparable with the cadences of virulence so characteristic of the diphtheria bacillus and other epidemic organisms.

We emphatically do not desire to convey the impression that the majority or even a great number of cases of pemphigus neonatorum have had their infection transmitted from their mother's milk. Since this method of transmission has not been a recognized one, it is enough for preventive purposes to show that it may *sometimes* occur; for it must be obvious that any number of babies might have been infected from this one mother, even while her own child was still rigidly isolated. In such event responsibility might have been directed toward those having direct charge of the infant's segregation, resulting in the same confusion that always occurs when the real source of infection and its transmission are hidden.

Summary. 1. The evidence submitted is at least presumptive that certain outbreaks of pemphigus neonatorum are traceable to an initial case infected by its own mother's milk.

2. Such findings occurred three times in sporadic cases that might have given rise to outbreaks had not the mothers been segregated, while in a third sporadic case with these findings an outbreak of ten cases actually did result.

3. A similar outbreak was also traceable to a burn infected with aureus, suggesting a diverse origin for the infecting cocci.

4. No epidemiological type could be associated with the disease, the organism being serologically the same as those isolated from abscesses, etc.

5. When the Staphylococcus aureus is rampant, as it has been for several years, it may be present in the milk and even in the blood stream of certain mothers with few or no symptoms, who may be viewed as "carriers."

6. The mild infection in one mother resembled in no way true impetigo, which fact fails to support the theory that pemphigus neonatorum and impetigo contagiosa bullosa are identical diseases.

7. By concentration of attention on this means of transfer we do not intend to minimize the predominant role played by case to case contact, undoubtedly the common method of transmission in institutions, but from a public health standpoint it would seem highly important to isolate both mother and child when it can be shown that the mother harbors the infecting organism.

SUPPLEMENTARY NOTE. Since this paper was submitted for publication some time ago it is of interest that we have had another single case of the disease. It occurred about December 1, and has been the only case since last June in an obstetric service that has about seventy-five deliveries a month. Furthermore, the nurseries are overcrowded.

The infant referred to had numerous pustules, but no constitutional symptoms. Staphylococcus aureus and albus were obtained in moderate numbers from both breasts of the mother. In this case the infant recovered without artificial feeding. The infection is undoubtedly mild enough in some cases that it is conceivable

that some infants might escape entirely if the number of cocci ingested was not too large. However, our control series have not happened to reveal such cases.

It is of note that careful segregation of both mother and infant has resulted in no further cases, after thirty days, despite the fact that several cases of Staphylococcus aureus sepsis and other aureus infections from the surgical departments have been in the hospital.

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SYSTEMIC REACTIONS TO ORAL INFECTION.*

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Biological Considerations. Even the most casual study of the relationship between general pathological processes and oral infection presupposes at the very least a certain knowledge of the origin and development of the teeth. Hertwig[1] says: "From a morphological point of view the teeth can well be designated as the most interesting structures of the oral cavity. Their development in man and mammal is accomplished in a manner which is neither simple nor easily intelligible; in the lower vertebrates, on the contrary, it is simpler." Mammalian teeth are limited in attachment to the entrance of the alimentary tube, whereas in the lower vertebrates teeth are characterized by a very wide distribution. Here they often cover not only the roof and floor of the oral

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cavity but occur also in immense numbers as palatal, lingual and pharyngeal teeth. They extend also in close-set rows over the whole surface of the skin, producing, as in the Selachians, a strong coat of mail. These primitive teeth are simply ossified papillæ of the skin and the mucous membrane, upon the contiguous surfaces of which they are formed. Shull,[2] speaking of the origin of teeth, says: "In some species (of the roundworm), tooth-like structures may be developed in the mouth cavity," and in the frog he states that the upper jaw bears teeth which serve to hold the prey when caught.

It is rather generally conceded that the organs which we commonly refer to as teeth, implying thereby masticatory function, phylogenetically are found first in the Selachians. Here the teeth occupy the edges of the jaw, serve for the comminution of the food and take their origin, not on the surface of the mucous membrane, but in its depths. However, in the Selachians the replacement of teeth by new ones throughout life is retained and remains as an unlimited process. Intense specialization of any organ bears a well-known relation to its function and to its stability. As the number of teeth in mammals have become reduced and as they have become more and more highly specialized, obedient to inexorable law, all that they have gained in function has been lost in power of replacement and of resistance to infection. Consider the highly specialized dinosaur, extraordinary in size, strength and structure, and the lowly modern crocodile, his sole remaining and decadent relative. The one took possession of the earth for a brief time, only to perish; the other lives on in slime because incapable of change.

Another biological consideration bearing upon the relation of the teeth to generalized human pathology is that of symmetry. The bilateral symmetry which characterizes all the higher forms, mammals in particular, has been undoubtedly evolved for the purpose of rapid motion. Man, cut by an antero-posterior plane, presents two mirrored halves. His sole asymmetrical system is the alimentary canal. Nor is this wholly without bilateral symmetry. No part of the body is more symmetrical than the teeth, both as regards distribution and bilateral identity of structure. The far-reaching importance of symmetry in animal form has been demonstrated by Hambidge,[3] who recently rediscovered the law of dynamic symmetry and its relation to the "whirling square." He proved that so seemingly divergent entities as the human skeleton and a Greek vase conform equally to this law. T. K. Hanna,[4] the well-known illustrator, states that the Egyptians were familiar with it and passed it on to the Greeks. The conformation of Greek art and architecture to the dynamic symmetry of living things is the fundamental explanation of their inimitable beauty. Deviations from this law, as in the case of asymmetrical dentition and asymmetrical antral development, are closely associated with liability to

infection. The recognition of such laws and of their applicability to the problems of modern medicine shows the trend of future research.

Originating in epithelium, which is the point of origin of all protective, secretory, excretory and absorptive organs, the teeth, as conceded above, and in common with certain other epithelial structures, are peculiarly liable to microbial invasion. This may be due also, in part, to their superficial position which often results in minute erosions. It is worth much more than a passing thought to note that most of the important areas of focal infection are of epithelial origin. It must be borne constantly in mind that the various systems of the body are intimately related and that no unit can be properly discussed as to form or function, without considering probable correlated involvement of one or more of the remaining units. Particularly in the consideration of oral infection there should be stressed the study of the *body as a whole.*

Reviewing these biological considerations, there are few if any structures in the body more ancient or more highly specialized than the teeth. For this they pay a price. Had they remained the simple, superficial, replaceable organ of the lower vertebrates, or higher invertebrates, there doubtless would be today no problem of oral infection. For the penalty of specialization is inexorable. The chambered nautilus has remained unchanged since silurian days, being rewarded for its lack of initiative by relative immortality. The commonplace is preserved, while exaggerations, good or bad, are swept away. As Shull, in discussing these problems says: "The paths of glory lead but to the grave."

Frequency of Associated Infections. It is rare indeed to find a patient suffering from focal infection in whom the areas of infection are not multiple. This doubtless was known to Billings, to whose clinical studies we owe much of our present knowledge of the fundamental cause of most disease syndromes; and also to Adami, whose pathological reseaches led him, twenty years since, to the promulgation of the well-known theory of "subinfection." The term oral infection properly implies not only dental and tonsillar lesions but also paradental infections. For the more one studies this problem of the sequence and the correlation of oral lesions the more convincing is the evidence that chronic maxillary sinusitis is not only very frequent in occurrence but is also often directly of dental and remotely of tonsillar origin. It is important therefore to look upon all the sinuses, clinically, as closely associated with the oral cavity. There is much evidence that sclerotic changes or a condensing osteitis developing in the structure of the maxilla will, in a large percentage of cases, spread to the contiguous floor of the antrum. Unless the degenerating tooth is removed, the end-result is likely to be chronic maxillary sinusitis. (See Fig. 1.)

Elective Localization and Susceptibility. As clinicians we have found this part of the problem extremely perplexing. To Vaughan[5] we owe much of our knowledge concerning specific ferments of the cellular components of the body. Roger,[6] of Paris, has also dis-

FIG. 1.—Chronic scleropurulent maxillary sinusitis (left), resulting from severe upper left peridental infection.

cussed this matter comprehensively, and in this country Rosenow has emphasized the law of specificity. Recently Price,[7] in a monumental monograph which bids fair to revolutionize our entire understanding of the importance of dental lesions, brings the matter up to the present day. Manwaring and Boyd,[8] studying bacterial toxins by means of the isolated mammalian heart, conclude that streptococcus filtrates are markedly toxic toward both the conducting and contractile tissues. Cotton[9] has demonstrated the relation of dental infection to insanity.

Summarizing these essays in terms of our own studies, it is clear that the organisms responsible for dental infection, particularly those of the so-called "rheumatic group," show a consistent and unvarying specificity in their behavior, not only toward the tissues of experimental animals, but toward those of man as well. It is well known that hereditary susceptibility is a factor of the utmost importance, when considering the specific relationship between "rheumatic group" organisms and lesions of the cardiovascular and joint tissues. That heredity and specificity are also of importance in considering lesions of the brain with its resultant functional disorders has been shown by Cotton. The mechanism for the production of toxic cerebral lesions is the same as for the production of "rheumatic" heart and joint lesions. In both cases the specific localization of the organism is aided by the inherited susceptibility of tissue.

Hemic Cellular Components. Considering the normal percentage of large and small lymphocytes to run from 21 to 38 per cent and the polymorphonuclear neutrophiles from 60 to 70 per cent,[10] in the average adult individual, it is evident that there are certain well-defined and definite changes in the relative proportion of these cells nearly always to be found in adult patients harboring focal infection. The occasional exception to this rule is probably due to the fact that the hemopoietic functions of the body have not yet been put out of equilibrium by the toxicosis. Bearing in mind the warning given by Bass and Johns,[10] that whenever the total number of a given kind of leukocyte is increased or decreased the percentage is affected accordingly and that what may be a low percentage for a given cell may in fact not indicate an actual loss of such cells, but on the contrary an increase in other cells or *vice versa*, we have analyzed our laboratory reports from 35 patients presenting definite evidence of colon-streptococcus focal infection with the following results: Average number of total leukocytes 6183; average percentage of polymorphonuclear neutrophiles 49 per cent and of lymphocytes, large and small, 45.6 per cent. A similar analysis of a group of 44 adults not presenting evidence of focal infections shows the average blood count to be as follows: Total leukocytes 8440; polymorphonuclear neutrophiles, 66 per cent and total lymphocytes, 33 per cent.

RELATIONSHIP OF ORAL INFECTION TO SYSTEMIC DISORDER

	Case No., sex, age.	Chief complaint.	Oral findings.	Other findings.	Treatment.	Result.	Remarks.
1	4281 M. 26	In 1916 constipation; headache; increasing drowsiness, incoördination, incapacity; personality deterioration; marked irritability. In 1922 bowels much better and generally improved, but not well	Not studied at this time; infected teeth, 8; chronic sclеropurulent sinusitis	Six-day delay in roentgen-ray emptying of colon; 9-hr. gastric emptying and terminal ileac delay; chronic pericolitis; segmental colitis; roentgen-ray of gall tract, moderate colon delay; tonsils infected	Subtotal colectomy, both right and left sides; 8 teeth removed; both antra opened and cureted; tonsillectomy	About 50 per cent improved; able to hold his job but no more; stationary for 6 yrs.; reëxamination in 1922, immediate improvement; cessation of all residual symptoms; is now running own business	Drug clerk; butt of ridicule for other clerks because of stupidity and quantity of castor oil taken; constantly demoted and about to be discharged as useless; colon should have been operated on last, not first; illustrates progress made in studying such cases as a whole.
2	5701 M. 77	Sudden alarming loss of vitality; had not been sick since early youth; generalized pain, sleeplessness and anorexia	Severe apical infection and peridental infection of 6 teeth; sinuses not studied	None at that time	All dental infection removed	Complete restoration to normal in 2 mos.	Farmer; life-long activity both mentally and physically; able to return to outdoor work and public speaking; sick again 5 yrs. later; tonsils removed; normal and improved at 80 yrs. of age.
3	4460 M. 50	Dyspnea on exertion; precordial pain; irregular heart; weakness; nervousness; insomnia	Very severe pandental infection; sinuses not studied	Cardiac arhythmia; true angina	Removal of all teeth and necrosed bone under general anesthesia	A temporary improvement in subjective symptoms	Sudden death 1 yr. later; sclerosis of coronary arteries and degeneration of the heart muscle.
4	5745 F. 47	Paranoid ideas; systematized ideas of persecution (toxic psychosis)	Infected teeth, 29	Tonsils infected	Tonsillectomy and 29 teeth extracted	Discharged in 5 mos.; economically independent; well for 3 yrs.	Two wks. after completion of dental and tonsillar work the psychosis ceased.
5	5484 F. 18	Pain in head (toxic psychosis); duration, 2 yrs.	Upper right molar and 2 other teeth infected; severe infection of right antrum	Tonsils infected	Tonsillectomy; rt. antrum opened, cureted; pus sac removed	Marked improvement, but not yet normal; 6 mos. since detoxication	Mental status indicated early dementia precox; removal of infection has arrested the psychosis.
6	5150 M. 56	Insomnia for 20 yrs.; early mental disorientation	Severe necrosis of left upper jaw surrounding devitalized molar; severe infection of left antrum	.....	2 teeth removed, bone cureted; the antrum opened and drained	Weight increased; sleeps very well; mentally keen 1 yr. later	Duration of jaw infection at least 20 yrs.
7	5158 F. 44	Shortness of breath; gas; impaired vision precipitated by pregnancy 6 yrs. ago; headache constant and severe	Eight infected teeth found in 1923	Infected tonsils found in 1919; usual signs of a chronic nephritis and cardiovascular deterioration; systolic, 175, diastolic, 110	Tonsillectomy in 1919 and 8 infected teeth removed in 1923	No marked improvement in symptoms; cessation of all subjective symptoms; restoration to active life	Never sick until acute nephritis in 5th mo.; induced labor saved her life, but nephritis continued; removal of tonsils alone insufficient to arrest deteriorative processes; points to necessity of removing *all* oral foci.
8	4653 M. 61	Headache; pain in both eyeballs; loss of sense of smell; "belly aches; "constipation; neuritis; cardiac arhythmia	Serious infection of rt. upper jaw; infected root in rt. antrum, sclerotic and infected	Hemorrhoids; pericolitis at splenic flexure; obstructive constipation	Surgical removal of oral infection; hemorrhoidectomy	Greatly improved	Abdominal and cardiac symptoms shown to be secondary to oral and anal involvement.

9	5893 F. 40	Rapidly increasing blindness; severe orbital pain	Edentulous; throughout life a severe dental infection; double maxillary sinusitis; chronic ethmoiditis	Double glaucoma; paracentral scotoma and cupping of disk of rt. eye; no intranasal pathology	Both antra opened, cureted and drained; infection was severe; double iridencleisis	One yr. later, permanent decrease in tension; intercurrent myopia disappeared in 3 mos.; pain ceased in 4 mos.	Chronic intestinal invalid for 20 yrs.; improved by hemicolonic exclusion 10 yrs. ago; total colectomy 3 yrs. ago; if infection caused eye lesions it began in teeth.
10	3987 F. 64	Chronic eye trouble 3 yrs.; total blindness of left eye 1 mo.; right eye nearly blind; severe nausea, vomiting and abdominal pain	Edentulous for 30 yrs.; maxillary osteomyelitis and necrosis; double maxillary sinusitis	Chronic uveitis; iridocyclitis; vision: O.S., 0; O.D., 29/200	Necrotic bone removed; both antra were opened by oral route, cureted and drained	Three days later able to distinguish buildings; in 3 wks. able to read 4th line of optic chart; in 1 yr. able to read ordinary print with right eye; left eye blind; abdominal symptoms improved	Important association of gastrointestinal and eye conditions and improvement in both; patient has gained 30 lbs. and for 3 yrs. past has been able to read and do al her own housework.
11	4026 F. 64	Arthritis and cholecystitis 10 yrs.; greatly disabled; hands nearly useless; in autumn of 1922, sudden pain, redness and diminished vision of left eye; nearly absent 4 days after onset	In 1921 dental infection found; rerayed; upper left 3d molar infected; severe left maxillary sinusitis and ethmoiditis	Almost constant pain and tenderness over gall bladder in 1922; iridoscotoma of left eye	Tonsillectomy in 1919 and 13 teeth were removed 1921; 3d molar removed; left antrum cureted and drained; later right antrum cureted and drained	Arthritis checked; G.I. symptoms slowly increasing; vision restored 1 mo. after antral drainage; great improvement in G.I. symptoms	Bad surgical risk prevented cholecystectomy; right tonsil drained into right axillary lymphatics; important relationship between all mental symptoms and oral infections.
12	5368 M. 70	Rapid and increasing loss of vitality; insomnia and headache; mental depression; pain in leg; Dupuytren's contracture of rt. ring finger 15 yrs.	Pyorrhea; severe peridental infection of both upper molar areas; severe double maxillary sinusitis	None	Infected teeth were removed; both antra opened orally, cureted and drained	Almost immediate disappearance of pain in leg; general health better; relaxation of Dupuytren's contracture	Symptoms arrested for 9 mos. recurrence of sinus infection and some symptoms; interesting relationship between oral infection and Dupuytren's contracture.
13	5627 F. 73	Severe diarrhea; duration, 4 mos.	Six devitalized teeth; severe pandental infection	Tonsils infected; 3d degree colitis with fibrosis	All dental and alveolar infection eliminated	Improved; occasional attacks of diarrhea	Each extraction followed by severe prostrating diarrhea.
14	5569 M. 39	Neuritis; spasmodic severe pain in left shoulder 4 wks.; sleeplessness; frequent disability both arms 10 yrs.	Devitalized infected upper and lower molars; sinuses negative	Colon stasis, 72-hr. total; tonsils out; w.b.c., 6800; polys., 23 per cent; lymphs, 72 per cent	Dental infection eliminated	Greatly improved after 2 mos.; sleeping normally; able to play	Elimination baths and electrothermic treatments made pain worse; severe blood-count inversion; roentgenray of shoulders negative.
15	5229 M. 20	Fatigue, mental and physical; irritability; personality deterioration	Two impacted 3d molars; lower angle of left antrum sclerotic	Infected tonsil stumps; trace of albumin; no casts; renal function, 75 per cent; 3 hrs.; cardiac hypertrophy; mitral insufficiency; blood-press., 175/125	Tonsil stumps were removed; impacted 3d molars removed	Marked physical and mental improvement; able to work on farm; blood-pressure 145/90	Important example of marked personality change in youth associated with extensive oral infection; had been high-grade scholar, now 3d-grade; permanent mental, moral and physical deterioration.
16	3934 M. 53	Severe attacks of pain in upper right abdomen; nausea, vomiting; acutely ill 6 wks.; indigestion 4 yrs., with jaundice, headache and loss of strength	February, 1921, 2 infected teeth and 2 areas of osteomyelitis; infected left antrum	Typical gall bladder tenderness	Two infected teeth removed; surrounding bone cureted; antrum cureted and drained	Gained 25 lbs. in 8 mos.; cessation of all abdominal symptoms	This patient would have been operated on for gall bladder had he not been a poor surgical risk; shows important relation of oral infection to abdominal lesions.

In attempting to explain this apparent inversion of the normal ratio between the cellular constituents of the blood, close scrutiny of all figures is necessary. The ratio between the polymorphonuclear neutrophiles and the total lymphocytes seems to indicate a decrease of the former and an increase of the latter. What occurs, however, is this: There has been an actual loss in cellular components, as shown by the total cell counts for the two groups. It is a fact, however, that, whereas the *percentage* of lymphocytes has changed, their *total number* is the same for both groups—while the

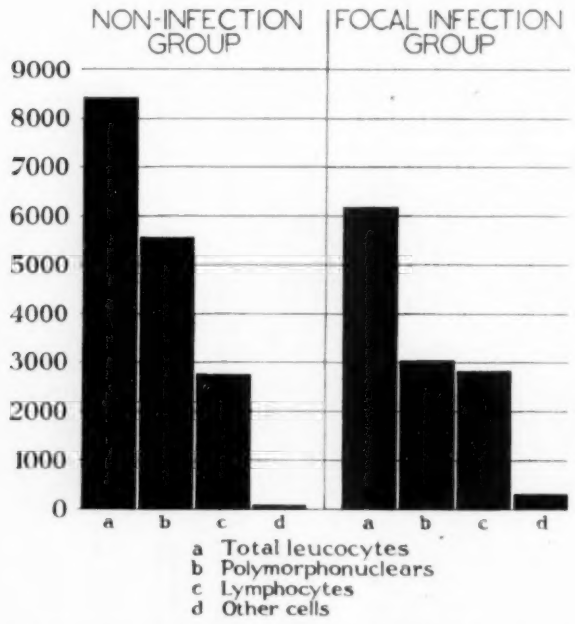

FIG. 2.—Chart showing average white-cell count of 44 adults not presenting evidence of focal infection, and of 35 adults presenting definite evidence of focal infection. Note (1) the decrease in total white cells in the focal-infection group; (2) the corresponding decrease in the polymorphonuclear cells, and (3) the absence of change in the lymphocytes.

total number of polymorphonuclear neutrophiles is decreased in the focal-infection group by an amount approximately equal to the difference between the total cell counts of the two groups. It is evident then, from these figures, that alterations in the blood picture of the focal infection group as a whole must be due to changes affecting chiefly if not entirely the polymorphonuclear neutrophile cells. (This is graphically shown in Fig. 2.) Just as in the acute febrile infections there is an increase in these defensive phagocytes, so in the chronic non-febrile infections there is finally

a marked reduction in their number. With constant extensive leukocytic infiltration about chronic infective foci, a point is reached where cell destruction exceeds cell regeneration. After reduction of the toxemia by mechanical means there is a definite tendency for the cellular ratio to return to normal.

Finally, in discussing the chart analysis of 16 patients (see Table), all suffering from remote and general pathological conditions due *chiefly* to oral infection, we would call especial attention to the following: (1) To the three instances in which blindness was considered by competent occulists to be imminent and in which the progress of the lesion was arrested by oral detoxication; (2) to

FIG. 3.—Showing relaxation of Dupuytren contracture eight months after oral detoxication.

3 patients in whom cardionephritic lesions predominated; (3) to 2 patients in whom insomia was the chief complaint; (4) to 2 patients suffering from well-defined psychoses; (5) to 4 patients presenting typical symptoms of gastrointestinal invalidism and who obtained subjective relief from oral detoxication; (6) to two patients suffering from neuritis, definitely arrested by the same procedure. An interesting observation upon one patient, No. 5368, consisted in the unexpected but definite relaxation which took place in a Dupuytren contracture of fifteen years' standing (Fig. 3).

On all hands the evidence appears to be increasing that dental infection stands in an important and until recently unrecognized causal relationship to many remote systemic pathological conditions.

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REVIEWS.

THE CURE OF PULMONARY TUBERCULOSIS BY REST AND EXERCISE. By HUGH M. KINGHORN, M.D. Pp. 169; 8 illustrations. Boston: Richard G. Badger, 1924.

THIS small volume deals with the rest treatment of tuberculosis in an interesting manner. There is a well-written account of the work of three pioneers in the treatment of tuberculosis, Brehmer, Dettweiler and Trudeau, which brings in the personality of these men in a way that makes this book really entertaining. A discussion of methods and results of treatment refers to the work of Paterson and Joseph Pratt. This book is well written, the subject briefly but thoroughly covered in a sound manner.

R. T.

CONTRIBUTIONS FROM THE PEKING UNION MEDICAL COLLEGE. Vol. III. Pp. 495; numerous illustrations. Peking, 1924.

THE thirty-eight articles making up this volume are ample evidence of the good work that has been done at Peking since the appearance of the second volume of contributions in 1922. Most prominent are the biochemical papers by Read, Wong and Wu, together with the important article on gas and electrolyte equilibria in the blood by van Slyke, Wu and McLean. Two papers by Detwiler on spinal cord experiments in Amblyostoma are also noteworthy. The formist will regret that the back of each of the three volumes differs from the others.

E. K.

ANATOMISCHE PRÄPARIERÜBUNGEN. By HANS VON VIRCHOW, Vol. I. Cloth: Price, Marks 4.00. Pp. 66; 13 illustrations. Vol. II. Cloth: Price, Marks 5.50. Pp. 110; 13 illustrations. Berlin and Leipzig: Walter de Gruyter & Co., 1924.

THESE two little dissecting manuals are from the pen of a well-known anatomist, who embodies in the text the methods used in

his institute. The booklets are intended as a guide for the student while he is actually at work. The contents are logically arranged, the descriptions clear and to the point; many "remarks" indicate the practical applications. While Professor Virchow's books will no doubt be well received by students in German Universities, there are so many excellent dissecting guides in English that a new work on this subject would have to be of exceptional merit to supplant those in use in American schools. B. L.

THE CHEMISTRY OF THE BLOOD IN CLINICAL MEDICINE. By O. L. V. DE WESSELOW, M. B., F.R.C.P., Chemical Pathologist and Physician to Out-Patients, St. Thomas's Hospital, London. Pp. 255; 12 illustrations. London: Ernest Benn Limited, 1924.

THIS is the most satisfactory book on this subject from several points of view which the reviewer has had the pleasure of seeing. For the practitioner who desires a brief, clear statement of the chemical aspects of blood chemistry, this book can be heartily recommended. For the teacher of biochemistry in the medical school who has little contact with the clinical problems of the practitioner this book will serve as a reminder of the practical applications of the science which he is teaching. In the 255 pages of the book there are included chapters on each of the important phases of the chemistry of the blood; first the chemistry of the normal blood and then a consideration of the changes which occur in diabetes, nephritis, acidosis, alkalosis, hyperemia, etc. Especially is the chapter on acidosis clear, concise and eminently sane. One might perhaps find fault with the use of the old CO_2 capacity method as described but other than this no possible criticism of the book can be made. O. P.

THE EXTRAORDINARY EXPLOITS AND EXPERIENCES OF MUNCHAUSEN, M.D. By JULIAN WALTER BRANDEIS, M.D. Pp. 229; numerous illustrations. The Quip Publishing Company, 1924.

A RATHER dismal attempt to apply Munchausen with a dash of Mark Twain to modern medicine. Hypnosis-anesthesia, endocrinology, psychoanalysis, eugenics, cancer cures and similar topics are trotted out only to show very halting paces. Munchausen's self-rescue from a deep chasm by picking the fruit of the Pissepewa tree on which he was suspended and the general practitioner's device for preventing his practice from falling into the hands of the specialist are welcome though small oases in the arid desert. The illustrations are about as good as the text. E. K.

DEVELOPMENTAL ANATOMY. By LESLIE B. AREY, Professor of Anatomy at the Northwestern University Medical School, Chicago. Pp. 433; 419 illustrations. Philadelphia and London: W. B. Saunders Company, 1924.

UNDER the above title, we have a new presentation of the Prentiss text-book of embryology, of which Professor Arey was editor and co-author for some years. He has virtually rewritten the book, has rearranged the order of the various topics, and has made minor additions to bring the information up to date. The dissection of the pig embryos, ranging in size from 5.5 mm. to 35 mm. remains as one of the unique features of the book. The use of these dissections has added greatly to the interest of embryology as a laboratory science, and serves to render concrete certain developmental processes. As a well-written and well-illustrated text-book, it will meet with continued success under Professor Arey's authorship.

W. A.

REGENERATION FROM THE PHYSICOCHEMICAL STANDPOINT. By JACQUES LOEB. Late Member of the Rockefeller Institute for Medical Research. Pp. 143; 115 illustrations. New York; McGraw-Hill Book Company, 1924.

THIS was one of the last works from the experimental laboratory of Jacques Loeb, the eminent biologist. Using the plant Bryophyllum of the Bermudas, he studied why mutilation or wounding of an organism gives rise to phenomena of growth which do not occur without mutilation, and why the new growth frequently results in some kind of restoration of the old form. He was able to show a quantitative relation between the mass of the original plant substance and the mass of the regenerated part. The work lies in the domain of general physiology, and is one of the first attempts at a quantitative investigation of the phenomena of regeneration.

W. A.

ZEITSCHRIFT FÜR MIKROSKOPISCH-ANATOMISCHE FORSCHUNG; Vol. I, Parts 1 and 2; PROF. H. STIEVE, University of Halle, Editor. Pp. 351, 6 plates and many text figures; Akademische Verlagsgesellschaft M. B. H., Leipzig, 1924.

THE condition of scientific periodicals in Germany for the last few years has been a matter of considerable interest. Certain journals have been discontinued, others have joined forces, considering it better to continue as one successful journal than as two struggling under difficulties. At the present time fresh activity is observable, and among the new journals resulting is the above-

named one. The desirability of having a new journal for histology has come about through the amalgamation of the Archiv für Mikroskopische Anatomie with Roux' Archiv für Entwickelungsmechanik. The resulting journal, under the editorship of Roux, contains articles on biological topics, mainly experimental in nature. The Archiv für Mikroskopische Anatomie was for sixty years the place of publication of the most noteworthy researches in histology, and as the character and identity of this journal has been lost by its union, there came the need for a journal of similiar content and scope. In the two parts of the new journal which have appeared there are ten articles, of which four are from the editor's own laboratory, and all of great interest. There are eight assistant editors, representing well-known anatomical centers such as Utrecht, Berlin, Zurich and Upsala. One may safely predict a successful future for this new contemporary. W. A.

THE MEDICAL RECORD VISITING LIST OR PHYSICIANS' DIARY FOR 1925. Pp. 300. New York: William Wood & Co.

THIS useful pocket notebook is designed for recording visits, charges, etc. The first few pages contain tables of dosage and other miscellaneous data. J. A.

PRACTICAL LECTURES, DELIVERED UNDER THE AUSPICES OF THE MEDICAL SOCIETY OF THE COUNTY OF KINGS, BROOKLYN, NEW YORK. (1923–1924 Series.) C. A. GORDON and T. S. WELTON, EDITORS. Pp. 484; 135 illustrations. New York: P. B. Hoeber, 1925.

THE Kings County Medical Society, wishing to celebrate its one hundredth anniversary by a demonstration of public service, decided to arrange a series of practical lectures on topics chosen by its committee, "believing that continuous education of the practising physician would be the greatest possible contribution that the Society could make in the cause of public health." The twenty-five lectures were so successful that it was thought advisable to publish them. The surgical and obstetrical topics predominate—the "surgical abdomen" (eheu!), surgical diagnosis, appendicitis and similar topics are presented by such well-known men as Blake, Deaver and Polak. Medical topics—such as renal function, chronic arthritis, bacterial endocarditis and epidemic encephalitis are covered by Mosenthal, McCrae, Libman, Tilney and others, with one lecture each on common skin diseases by Fordyce; every day bacteriology by Oliver; rational pathology by Ewing, and medical psychology by Walsh. E. K.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Antirachitic Properties Imparted to Inert Fluids and to Green Vegetables by Ultraviolet Irradiation.—Following up the recent lead obtained when it was discovered that ultraviolet irradiation of cod-liver oil increased its antirachitic property, HESS and WEINSTOCK (*Jour. Biol. Chem.*, 1924, **62**, 301) now report similar studies on a variety of substances and foods. Such inert fluids as cottonseed and linseed oils become active antirachitic agents after irradiation *in vitro*, and they retained this property for a considerable period. Wheat grown in the dark was valueless in this regard, but when grown in sunlight or irradiated with ultraviolet light it was strongly protective. Vegetables irradiated, either before or after being plucked, showed a very marked increase in their antirachitic property. This would definitely point to the uselessness of green vegetables grown under glass in winter as sources of protection against deficiency diseases.

Modification of Diphtheria Toxin by Formaldehyde.—GLENNY and HOPKINS, in 1923, first showed that diphtheria toxin could be so modified by the action of formaldehyde that the specific toxicity was greatly reduced while the binding power for antitoxin remained unchanged. The present paper by GLENNY, HOPKINS and POPE (*Jour. Path. and Bacteriol.*, 1924, **27**, 261) deals with further details of this formalization and the use of this altered toxin for immunization. The amount of formaldehyde required to render a given toxin preparation nontoxic depends greatly on the amino-nitrogen content, as was to be expected, since this is where the bulk of formaldehyde goes. Such nontoxic toxin may have its total combining power for anti-

toxin little affected, but the speed of this combination is greatly lessened. By acid precipitation of the altered toxin they were able to obtain as much as a forty-fold greater combining capacity for antitoxin in comparison to the amount of amino-nitrogen present. This concentrated formalized toxin they found to be far superior to ordinary toxin for active immunization against diphtheria and in the commercial production of antitoxin. The immunity to the disease appears earlier (in rabbits as early as nine days, in guinea-pigs eleven days) and is of a high degree.

Immunological Significance of Vitamins.—In their earlier work WERKMAN, BALDWIN and NELSON failed to account for the decreased resistance to infections in animals on a deficiency diet on the basis of altered antibody production or reduced bactericidal power of the blood. They did find a lowered body temperature and reduced phagocytosis in these animals, and thought these findings of some significance. They have now (*Jour. Infect. Dis.*, 1924, **35**, 549) studied the effect of a deficiency diet (B vitamin) on the resistance of rats to diphtheria toxin. They found an increase in the susceptibility of the rats to the toxin, death following the injection of doses much below the lethal amounts for rats on normal diets. Even with this susceptibility the rats did not show a lowered antitoxin production. The principal cause of the greater toxicity for these avitaminic rats lay in the effect of the toxin on the blood pressure. A marked and sudden drop in pressure occurs usually on the second or third day after the injection, and is progressive until death intervenes. A mere lack of vitamin B alone serves to cause a progressive fall in blood pressure. The increased susceptibility to diphtheria toxin apparently lies in its augmentation of this already abnormal state.

SURGERY

UNDER THE CHARGE OF

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Common Duct Stones and Primary Suture of Common Duct.—ELISCHER (*Centralbl. f. Chirurgie*, 1924, **49**, 2690) says that suturing the common duct is contraindicated only in the brittle, thin-walled type of common duct. This procedure was followed in 16 selected cases in a series of 86 cases of stones in the common duct. In the remaining 70 cases drainage and palliative operations were performed. Thirteen persons in the series of 16 gave history of jaundice, while all showed bile in urine at time of operation. Seven showed fever at time of attack.

The stones were solitary stones in 14 patients, 7 were incarcerated in the region of the papilla, while 7 were movable. One case showed 2 stones, while the remaining case showed several faceted stones. There were 2 tiers of sutures and a fine capillary drain was carefully inserted alongside. The author stresses the fact that drainage and short circuiting operations should be used in strict emergencies—while the procedure described should be used in carefully selected cases.

The Effect of Ligation of Branches of the Renal Artery.—BELT and JOELSON (*Arch. Surg.*, 1925, **10**, 117) say that the changes produced in the circulation of the kidney following ligation of one of the larger renal arterial branches are closely portrayed by means of the celluloid injection method. An almost absolute ischemia confined to the region supplied by the blocked vessel is followed by a late ingrowth of small anastomatic channels into the bloodless area. These increase in size up to the fifth week, after which time scar-tissue formation, resulting from the effects on the stroma of the long period of ischemia, again makes the area relatively avascular. The end-result is a depressed stellate scar equal in area to the region supplied by the ligated branch. The clinical significance of this is self-evident. Although in renal surgery it may at times be necessary and justifiable to divide one of the large branches, it should be borne in mind that such a procedure causes a necrosis of the area of renal parenchyma supplied by that vessel. While this necrosis may not be of a magnitude which will result in clinical evidence of renal insufficiency, still it does definitely decrease the amount of renal reserve tissue, for restoration of function in such areas is shown to be anatomically impossible.

Postoperative Massive Collapse of Lung.—SCOTT (*Arch. Surg.*, 1925, **10**, 73) states that postoperative massive atelectasis presents a striking clinical syndrome and is relatively frequent. It is differentiated from all other acute conditions by displacement of the heart and mediastinum toward the side that shows evidence of pulmonary consolidation. Asymmetry of the chest, unilateral limitation of respiration and cyanosis are early and striking signs. Latent cases occur, which are nearly symptomless and others are so severe that they resemble pulmonary embolism. The prognosis is excellent. Massive atelectasis may be complicated by bronchopneumonia and in this group the fatalities occur. The mechanism of massive atelectasis appears to be a reflex blocking of the finer air passages in the affected lung tissue, quite possibly of vasomotor origin. Collapse of lung tissue after operation seems to be a significant element in other pulmonary complications.

The Surgical Treatment of Paralytic Deformities of the Foot.—MAYER (*Amer. Jour. Surg.*, 1924, **38**, 289) believes that first progress in treatment of these deformities came in tendon transfer. Further improvement was made by operations, dealing with reconstruction of the bones of the foot. Whitman's operation of astragalectomy, combined with posterior displacement of the foot, gives a suitable foot even when most of the muscles of the calf are paralyzed. It has, however, the disadvantage of shortening the extremity from ½ to 1 inch. G. G. Davis advocated a subastragaloid arthrodesis combined

with a posterior displacement of the foot. Michael Hoke published a stabilizing operation in 1921. His operation reshapes the head and neck of the astragalus in such a way as to overcome the deformity and arthrodeses the joints between the astragalus, scaphoid and os calcis so as to maintain the bony relationship in any position that the surgeon desires. In milder forms of flat-foot, there is weakness of the tibialis anticus muscle, but the other invertors of the foot are strong enough to prevent the development of marked deformity. This type alone can be improved by non-operative measures. Outspoken paralytic flat-foot, paralytic club-foot and paralytic calçaneocavus are treated by various combinations of tendon transference with stabilizing operations upon the bones of the feet. The author stresses careful grading of the deformity according to the muscles paralyzed and the degree of deformity. In very mild cases non-operative measures were sufficient; in the moderate grade tendon transference was done; in the more marked cases tendon transference was combined with bone reconstruction.

Surgical After-Treatment in Thyroid Disease.—DEAVER (*Amer. Jour. Surg.*, 1924, **38**, 296) says that every means of treatment known to be of real value in the postoperative care of thyroid cases should be available for reference when needed. Operative mortality in goiter work may be lowered by individualizing every case. The patient's resistance should be at the highest available point. Obesity, excessive summer heat, great loss in weight, a rapid pulse, which will not slow down under rest, but rises quickly on the slightest exertion, are danger signals, even with a low metabolic rate. Five things are essential in every operative goiter case. They are rest of body and mind, a reconstructive diet, sufficient elimination, free ingestion of fluids and carefully directed medication. Iodin aside from its use in simple and adolescent goiter, may, according to Plummer, have a special indication in the exophthalmic form, either before or after operation or both. Postoperative simple goiter usually runs a quiet course. The exophthalmic type may manifest a rather varied reaction merging from a mild form into that which is stormy or even violent. Water should be given from the start, regardless of vomiting. Cerebration must be subdued and renal function encouraged. Cold externally is often of great value. Of drugs, the most important are luminal, bromides, morphin, digitalis and in selected cases, iodin. Collapse of the wind-pipe and grave secondary hemorrhage are the tragedies of goiter surgery. Recurrence in simple goiter may be compensatory in young persons, and may therefore subside. If it persists, medical or surgical treatment is advised. Recurrence in the toxic or exophthalmic form, calls for further removal as a rule. The advanced exophthalmic case with fixed complications cannot be completely cured. Every operative goiter case, simple or toxic, should be kept under observation until the best possible results have been reached. Advice and treatment from too many sources should be discouraged.

Malignant Epithelial Tumors of the Thyroid.—GRAHAM (*Surg., Gyn. Obstet.*, 1924, **39**, 781) declares that at least 90 per cent of malignant tumors arising from thyroid epithelium have their origin in preëxisting

adenomata. The morphological character of the cells and tissue is an unreliable basis for the determination of malignancy of thyroid epithelial tumors. The malignancy of thyroid epithelial tumors depends upon their tendency, or capacity to invade the capsule, surrounding tissue, lymphatics or bloodvessels. The most constant single indication of thyroid epithelial malignancy is invasion of the bloodvessels. Scirrhous and papilliferous adenocarcinomata are the only two types of epithelial malignancy in which invasion of the bloodvessels has not been observed. Epithelial tumors that are encapsulated are benign, irrespective of their microscopical appearances otherwise. Epithelial tumors, in which one finds invasion of the bloodvessels cannot be regarded as entirely harmless, irrespective of their microscopical appearances. The term carcinoma is proper for epithelial tumors of the thyroid that are malignant, regardless of their microscopical appearance. The term malignant adenoma is useful and convenient for the purpose of denoting a subgroup under carcinoma.

THERAPEUTICS

UNDER THE CHARGE OF

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Treatment of Asthma with Autogenous Vaccines.—THOMAS and TOUART (*Arch. Int. Med.*, 1924, **34**, 79) report the results obtained in the treatment of 62 cases of asthma by means of autogenous vaccines. Treatment was based on the results of reactions to intracutaneous tests with autogenous vaccines after preliminary routine tests for sensitization to foreign proteins had been made, and surgical treatment given to those cases which showed abnormalities of the nasopharynx, nasal sinuses, tonsils or teeth. The important factors in the use of vaccines were: (1) Proper selection by the intracutaneous test; (2) preparation of each organism in a separate vaccine; (3) the use of a therapeutic dose just sufficient to produce a mild local reaction; (4) adherence to this dose so long as it continues to produce such a reaction; then increasing it; (5) frequent dosage early in the treatment with a gradually lengthened interval, followed by (6) prolonged administration at relatively long intervals. The method of testing with autogenous vaccines described by THOMAS, FAMULENER and TOUART (*Arch. Int. Med.*, 1924, **34**, 85) depends on a standardization of vaccine based on the HOPKINS method (*Jour. Am. Med. Assn.*, 1913, **60**, 1615) in which a 1 per cent suspension in physiological sodium chlorid solution is prepared from the measured packed bacterial residue, and composes the stock vaccine. A unit consists of that amount of bacterial substance which is present in 0.01 cc of a 1 per cent suspension, and this quantity has been found to be the most favorable amount to produce a skin reaction when applied intradermally in a sensitive patient. Positive reactions may appear within ten to thirty minutes or in twelve hours and persist from two to

five days. Test vaccines were made from organisms isolated from tonsils, nasal sinuses, pharynx and stool. Treatment vaccines were prepared from the stock vaccine and contained approximately 1,000,000,000 organisms per cc. The initial dose was 100,000,000 organisms of each type selected. If a local reaction occurred it was repeated at intervals of two or three days until none followed. Then the dose was doubled on each injection until the desired result was obtained. Seldom did the dose exceed 400,000,000 organisms. With improvement in symptoms the interval between injections was increased first to five, later to seven days. Weekly, bi-weekly, or monthly injections were given after relief of symptoms and physical signs occurred because of the tendency to relapse. Of the 62 patients treated 53 have been either completely relieved or materially improved.

The Question of the Practical Significance and the Treatment of Extrasystole.—In the great majority of cases cardiac extrasystole is not dependent upon organic changes of the heart muscle, but is a functional disturbance of the heart. In most cases the prognosis is favorable, and SCHULTZ (*Deutsche med. Wchnschr.*, 1924, **40**, 1357) emphasizes the importance of determining by the electrocardiograph whether the cardiac irregularity is due to extrasystole or is a perpetual irregularity of the heart due to auricular fibrillation. He summarizes briefly the various opinions of eminent heart specialists, and their choice of treatment. Digitalis is usually of no use although small doses are sometimes beneficial aside from its effect as a general tonic. Other physicians use quinin and quinidin both of which substances cause a diminution of cardiac irritability. For the large majority of cases no medication is indicated, but elimination of deleterious influence and cure of insomnia.

A New Diet for Peptic Ulcer.—COLEMAN (*Jour. Am. Med. Assn.*, 1924, **83**, 885) reports a new diet for peptic ulcer which has been used for twelve years and given satisfactory results. Fat is given in the form of olive oil or unsalted butter, protein is supplied by egg white, and carbohydrate by rectal enemata of glucose solution. At the onset of treatment the patient is put to bed, the alimentary tract cleaned out by castor oil or some other laxative, and for from three to five days no food is given by mouth. Water is supplied by the enemata, and if these do not control thirst 1 to 3 ounces of water at room temperature may be given by mouth. After a daily enema of soapsuds 300 cc of a 10 per cent glucose enema is given by the drip method and repeated two or three times during the day. On the fourth to sixth day feeding by mouth is begun. One and a half to 2½ ounces of chilled olive oil alternating with the whites of 3 to 4 eggs every two hours is given the first day, increasing to a maximum of 150 cc of olive oil and 6 to 8 egg whites daily. To those patients who are unable to take olive oil unsalted butter, egg-yolk or cream in corresponding amounts may be given. That is 6 ounces of butter equals 5 ounces of olive oil or 2½ ounces of cream. Eight grams of salt are given in the food daily to prevent loss of chlorine from the body. This diet is continued for three to four weeks and for many months afterward only specially selected foods are given. The object and advantages of this diet is to give foods which do not incite gastric secretion and which least stimulate the

motor activity of the stomach. Gastric distress subsides quickly after treatment is begun, and in no instance was it necessary to give drugs to accomplish this result.

Autoserotherapy in Pleural Effusion.—MARCOU-MUTZNER (*Monde méd.*, 1924, **653**, 600) advocates autoserotherapy in pleural effusions as first used by Gilbert of Geneva rather than thoracenthesis with artificial pneumothorax. The former method he has used successfully for twenty years in every case of pleurisy with effusion whether tuberculous or not, and has seen no bad effects. After 2 or 3 injections of serum there is a marked diuresis and disappearance of the effusion. He has never seen a cold abscess develop, but does not approve of reinjection of pus, although clear or bloody fluid may be reinoculated. At the site of puncture without withdrawing the needle from the skin 2 cc. of pleural fluid is reinjected subcutaneously. This procedure is repeated every two days, and after a mild reaction there follows a marked diuresis, feeling of well-being, with diminution of the exudate. The greater the effusion the more rapidly one obtains beneficial results, and in the long-standing cases results are less marked than in the recent cases.

PEDIATRICS

UNDER THE CHARGE OF

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The Significance of the Presence of the Nephrogenic Zone of the Kidney in the Normal and the Syphilitic Fetus and the Newborn.—MEBANE.—(*Am. Jour. Dis. Child.*, 1924, **28**, 668) made histological studies of the normal kidney in 162 fetuses and newborn infants, and he found that the development of the renal tubules is completed when the infant is between 45 and 48 cm. in length. At birth in the full-term infant, which is from 48 to 52 cm. in length, the growth zone, or nephrogenic zone, of the kidney is absent. The nephrogenic zone is usually absent when the weight of the dead fetus is more than 2500 gm. The study of the kidneys in 14 patients with congenital syphilis failed to show in a single case a retardation in the development of the kidney with a persistent nephrogenic zone. In congenital syphilis, the nephrogenic zone disappeared at the same time as it did in the control series, when the infant was between 45 and 48 cm. in length. The presence of the nephrogenic zone is almost certain evidence of prematurity. Its prominence, whether slight, moderate or marked, may give some idea of the age of the fetus.

Endocrinology in Pediatrics, with Special Reference to the Hypoplastic-Dyspituitary Type of Child.—DOWD (*Arch. Ped.* 1924, **41**, 801) reports a number of cases, and comments that persons of all ages may be

abnormal or inadequate because of glandular deficiencies. Children of the status thymico-lymphaticus type, frequently overweight, sometimes tall, slender and loose-jointed, are a difficult problem of adjustment. The nature of their growth and development renders them frequently self-conscious, inadequate, prone to injury, and with a low resistance to infection. They can be assisted more rapidly to a condition of normality by a study of their internal secretions, with the administration of the appropriate glandular extracts, than by neglecting these glands and relying entirely on measures relating to diet and hygiene and correction of physical defects. Even the cretins are not the simple case of thyroid deficiency that they have always been considered. They are hypoplastic and their trouble is a pluriglandular one. Such conditions as epilepsy have some relationship to disturbance of internal secretion that warrants further study. Pituitary extracts have a distinctly favorable influence on fatigue, and on such symptoms as headache and bed-wetting when used in proper amounts and can aggravate the condition if overdose is given. Caution must be observed in the use of glandular extracts. Thyroid should be used in small doses, while pituitary whole gland and the anterior lobe extracts can be pushed unless the headache ensues, which was previously absent, or the existing one is aggravated. In some cases the enuresis will be aggravated rather than improved if too much extract is given. In the addition to the administration of these extracts by mouth, they may be given by injection with benefits in selected cases. Ovarian and testicular extract are useful when puberty is delayed. Large doses of pituitary extracts are not indicated when the sella is small and enclosed, or severe headache will follow. Rest periods when dosage is omitted are necessary from time to time. It is a temptation for the user of gland therapy to believe it to be the proper method of therapeusis in all kinds of cases. Such a feeling is unfounded. A great deal of good can be done by this treatment with the proper selection of the case, dosage and frequency of administration.

Residua and Sequelæ of Epidemic Encephalitis.—GOODHART and COTTRELL (*Jour. Am. Med. Assn.*, 1925, **84**, 32) says that human intelligence, comprehending the activity of the mind as a whole, includes the capacity of reception, assimilation and criticism. It is biologically dependent in large measure on the gray mantle of the brain. The emotions, strictly speaking, are referred to for their physical components to parts of the subcortical level, thalamus and corpus striatum, and are probably associated with both conditional and unconditional sensorimotor reflexes. When one considers the graduated disturbances of intellect and emotion that have appeared so strangely associated in postencephalitis and have affected attention, the higher sensations and the higher psychic combination processes, including those of critical judgment, imagination and creative power, it is a fair ground for assumption that all of these faculties are associated with the same brain segments that are functionally the seat of emotional reactions. The further painstaking investigation of encephalitic patients may yet give us information as to the function of the subcortical brain segments, and furnish valuable biological data with respect to the emotions and the higher creative processes. They analyze a series of cases. In a

study of the static, kinetic and synergistic mechanisms affected in encephalitis, and in such classified entities as chorea, dystonia musculorum, striatal syndromes, paralysis agitans and multiple sclerosis, not only is it indicated that the damaged nerve centers are the same anatomically, but also it is suggested that the acute pathologic condition in the one case terminates in a histopathologic process which is the same in the chronic stages of encephalitis as in the conditions that obtain in the syndromes of older nomenclature. A review of histories and observations does not suggest a more or less constant relationship between the symptoms of the acute illness and the development later of a particular type of motor deficiency.

A Study of the 1923 Epidemic of Anterior Poliomyelitis in Kansas.—Diveley (*Jour. Am. Med. Assn.*, 1925, **84**, 85) made studies of the data of the antero-poliomyelitis epidemic. If an early diagnosis is made and proper treatment instituted during the febrile stage, the resulting cord involvement is not only lessened, but in a great measure prevented. If proper treatment is carried out during the second or convalescent stage, from 75 to 85 per cent of the cases show marked improvement or complete recovery, against 40 to 45 per cent of partial recovery if proper treatment is not carried out. If proper treatment is carried out during the first and second stages, fully 90 per cent of the deformed limbs and backs can be prevented. Many cases recover spontaneously without treatment, while others still show signs of paralysis after one year of careful supervision. There are definite anterior poliomyelitis carriers. The infection is selective, and may run through neighborhoods or families, picking out various individuals. Most persons in a community during an epidemic have the disease in the light or abortive form, which gives immunity.

The Dick Test and Active Immunization with Scarlet Streptococcic Toxin.—Zingher (*New York State Med. Jour.*, 1924, **24**, 915) regards the Dick test as being a reliable method for determining susceptibility and immunity to scarlet fever. In his experiences with the test in more than 7700 cases, 8 positive reactors and none of the negative reactors have developed scarlet fever. The rapid appearance of the reaction in from eight to twelve hours is of great clinical value for this purpose. The Dick test helps in the diagnosis of doubtful cases of scarlet fever. In 232 cases of scarlet fever the Dick test showed that 91.3 per cent gave positive reactions during the early stages of the disease and negative reactions during convalescence. There were 19 patients who gave a persistent positive reaction, of these 2 developed scarlet fever subsequently. Of the remaining cases to the number of 17, 12 did not desquamate.

Tetania Parathyreopriva and Idiopathic Tetany; Functions of Parathyroids.—Paton (*Edinburgh Med. Jour.*, 1924, **31**, 541) produces evidence that apparently shows that the increased muscular tone which generally follows removal of the parathyroids indicates that these structures exercise an influence on the tonus of skeletal muscles. The marked increase of muscle tone, and the close similarity of the other symptoms to those produced by removal of the parathyroids which

follows administration of guanidin and its methyl compounds seems to show that they play a part in the maintenance of that tone. The fact that these substances are increased in the blood and urine after parathyroidectomy, and in the urine in idiopathic tetany suggests that metabolism is controlled by the parathyroids and that it is through them that muscular tone is regulated. The immediate action of these substances in one adequate dose is undoubtedly to stimulate the efferent neurons of the spinal cord, and in a moderate dose to increase the excitability of the neuromyons. With repeated doses, they apparently become anchored on these structures to produce a condition of facilitated activity and this probably is their chief mode of action in tetany. That a decrease in the calcium of the blood is not the primary factor in the causation of the symptoms is shown by the effect of bleeding and transfusion of a calcium-free solution, and further by the fact that a decrease of the calcium in the blood may occur without tetany. There is no conclusive evidence to show whether this fall, when it occurs, is a result of the increase in the methyl-guanidin or a concomitant with it. There is no indication that the increase in phosphates plays a direct part in the production of symptoms.

Obesity in Children.—Langmead and Calvert (*Lancet*, 1924, **2**, 1111) have found that the blood-sugar curves in cases of great obesity in children are diverse in their outlines. Their experiments appear to show that pituitary gland substance given by mouth is not inert. As far as carbohydrate metabolism goes, the blood-sugar curve being used as an index, it seems logical to administer that lobe of the pituitary which produces the better effect, on sugar tolerance. Considering the cases generally, the whole gland gives quite good results. The results of the experiments taken collectively might be construed as indicating that a properly blended pluriglandular therapy in cases such as these would be beneficial. Thyroid extract may reduce weight in cases of this kind, but it can hardly be considered as a safe remedy because it does not restore carbohydrate metabolism to normal. Possibly the reduction of the blood sugar may be an useful guide.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

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Simultaneous Vernes and Wassermann Tests for Syphilis.—Baylis, Sheplar and MacNeal (*Arch. Dermat. and Syph.*, 1924, **10**, 306), having made an investment in the elaborate equipment required for the performance of the Vernes precipitation reactions, report that the method is a distinct contribution to the exact reading of precipi-

tation tests for syphilis. They conclude that exact mechanical control is possible throughout the procedure by the use of the mixing and dropping apparatus, and that more objective and exact quantitative results are possible than with any other flocculation method. They regard the test as an important check on the Wassermann reaction, but evidently do not accept it as a substitute for the Wassermann procedure which gives more delicate shades of reaction between reagin and antigen.

Incidence of Mixed (Syphilitic and Chancroidal) Infections.—VONDERLEHR (*Arch. Dermat. and Syph.*, 1924, **10**, 314) states that 58 per cent of 98 cases of so-called chancroid gave a positive blood Wassermann test on an average of seven and a half months after the development of the venereal sore. Typical chancres are 1.25 times more prevalent than the non-syphilitic venereal sores. Mixed infections are 1.38 times more prevalent, and venereal sores that are syphilitic occur 2.63 times more frequently than the uncomplicated chancroid. Mixed infections constitute 38 per cent of all venereal sores, and their recognition by careful study at first appearance and subsequent Wassermann follow-up deserves emphasis.

An Experimental Study of the Prophylaxis of Syphilis with Arsphenamin, Neoarsphenamin and Sulpharsphenamin.—GREENBAUM and HARKINS (*Arch. Dermat. and Syph.*, 1924, **10**, 409) conclude, on the basis of animal experiments, using equivalent adult human doses of arsphenamin, neoarsphenamin and sulpharsphenamin, that a single curative dose equivalent to 0.9 gm. neoarsphenamin will not abort a syphilitic infection if given within three hours after infection. On the other hand three such doses administered on three successive days will abort the infection. It is advised, therefore, that three successive injections of twenty-four-hour intervals be given in the effort to abort a syphilitic infection immediately after inoculation.

Treatment of Ivy Poisoning by Rhus Tincture and Antigen.—WILLIAMS and MACGREGOR (*Arch. Dermat. and Syph.*, 1924, **10**, 515) conclude that the method of Strickler (*Jour. Am. Med. Assn.*, 1923, **80**, 1588) has greatly improved the therapeutic outlook in severe, fully developed cases of ivy poison. Before the dermatitis becomes marked thorough washing with soap and warm running water and applications of a warm slightly acidulated 1 or 2 per cent solution of potassium permanganate are effective. One year's trial of the Strickler method in the advanced cases has impressed the authors favorably. The antigen should be given in doses of 1 cc from the start, the intervals between injections varying from twenty-four to seventy-two hours. The larger doses were much more effective, and no ill-effects were observed. Rapid improvement usually followed the first dose.

Is Dandruff Seborrheal?—RULISON and HIGHMAN (*Arch. Dermat. and Syph.*, 1924, **10**, 429) frankly take issue with the common tendency to regard dandruff as a manifestation of seborrheic dermatitis. They review in some detail the evidence for the actual existence of an entity, pityriasis simplex, which they believe to be due to an infection with the

bottle bacillus of Unna. Upon this infection they believe a staphylococcic infection may be superposed. Seborrhea, on the other hand, is, according to the work of Sabouraud, caused by the microbacillus of seborrhea. Seborrhea produces permanent baldness, which it is almost impossible to prevent. Pityriasis produces a gradual thinning of the hair which is easily checked and re-growth may be expected. Seborrhea is not essentially a scaling disease, but pityriasis always is. One may have pityriasis in childhood, and at adolescence develop seborrhea, but in a combination of the two diseases the prognosis as to baldness is that of the more obstinate disease, namely, seborrhea. Infection with the gray staphylococcus (Welch's Staphylococcus epidermidis-albus) produces thicker, and more greasy, yellow scales, without the necessary production of seborrhea.

Calcium Content of the Blood in Various Diseases of the Skin, Based on Three Hundred Cases.—Schwartz and Levin (*Arch. Dermat. and Syph.*, 1924, **10**, 544), on the basis of a considerable series of cases and the review of literature, have concluded that with present methods of determining the calcium content of the blood no great importance can be attached to this item of blood chemistry in dermatology. They observed, however, some improvement from internal administration of parathyroid and calcium lactate in patients with low blood calcium in eczema and furunculosis. They found the calcium content of no importance in urticaria.

Scrofuloderma Gummosa (Tuberculosis Colliquativa).—Michelson (*Arch. Dermat. and Syph.*, 1924, **10**, 565) calls attention to a type of deep tuberculosis of the skin which begins independently of any underlying tuberculous process in other structures. The process is akin to the scrofulous gumma of the French (tuberculosis colliquativa), the diagnosis of which is always difficult, even if its presence is suspected. It is most likely to be confused with a syphilitic gumma, whose identity can only be recognized by histological examination. The process is more frequently seen in children and especially upon the face and neck. The author isolated tubercle bacilli in his case, but they are usually difficult to find in older lesions. He pertinently emphasizes Volk's warning that when the healing of a furuncle is unduly delayed one should be suspicious of a tuberculous process. A pseudofuruncular onset may mark these cases of tuberculosis colliquativa. The differential diagnosis includes syphilis and sporotrichosis. Tuberculosis is of a livid cyanotic blue, as distinguished from the rusty-red color of a syphilide.

Arsenic Cancer of Occupational Origin.—O'Donovan (*Brit. Jour. Dermat. and Syph.*, 1924, **36**, 477) reported three cases, all in sheep-dip workers. Sheep-dip contains, mixed with an arsenite of soda, both arsenic sulphide and free arsenious acid. The process of manufacture is very dusty, and the workers usually present arsenical pigmentation. The author gives the face, abdomen, scrotum, buttock, clavicle and lower chest as regions frequently affected. Arsenic cancer has been known since 1820. The constant presence of certain forms of arsenic on the skin in the form of dust can produce carcinoma cutis of the squa-

mous-celled variety. As in tar carcinomata, many years of exposure are needed. The replacement of manual by machine methods of handling, with instruction and periodic medical inspection of workers, does away with the disease. Early operation seems to afford a certain cure.

Fibrosarcoma of the Skin.—DARIER and FERRAND (*Ann. de Dermat. et de Syph.*, 1924, **5**, 545) discuss the clinical and histological picture and the treatment of the curious entity known to dermatologists as fibrosarcoma of the abdominal wall. These cases are comparatively rare, and consist in the development of nodular lesions in the skin about the umbilicus, more frequently in males than in females. Small, hard, fibrous nodules fuse to form a plaque, and later multiple tumors develop upon it. The larger lesions become slightly eroded over the surface. The process goes on for years, the lesions gradually breaking down and ulcerating with infection. There is no metastasis to neighboring glands and no involvement of the general health, the condition being purely local in character. Electrolysis and radium therapy are relatively ineffective, the resistance of the neoplasm being remarkable. Surgical extirpation of the fibrous plaque with all its tumors is the only procedure of value, and should be used as soon as the condition is recognized.

OBSTETRICS

UNDER THE CHARGE OF

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Extra-uterine Pregnancy at Full Term.—CATLIN (*Jour. Am. Med. Assn.*, 1924, **82**, 107) reports the case of a primipara whose last menstruation began December 12, 1921. Menstruation ceased and pregnancy developed and the patient felt well until January 25, 1922; she then had an attack of pain and faintness which recurred on the following day, and after that at intervals there was pain and some fever. This gradually became so severe that no food could be retained, and the bowels did not move for two weeks. She was then taken to the hospital, anesthetized and a pessary placed in the vagina to support the uterus. The pessary was kept in position for five weeks. After leaving the hospital there was another attack of severe nausea, after which the patient felt considerably better. Fetal movements developed, and the heart sounds were unusually distinct. After a period of unusual movement of the child the fetal movements ceased entirely. On examination the breasts contained a little secretion, the cervix was soft, but with no dilatation, and the body of the uterus could not be made out. There was a bruit on the left side of the abdomen, but no fetal sounds. Apparently the uterus contained a dead fetus, and it was decided to bring on labor by packing the vagina and cervix with

gauze. Four days later the patient was anesthetized and the cervix dilated, when the uterus was found empty. The patient was then removed to a hospital and a roentgen-ray showed the fetus in a sitting posture, with the head at the margin of the ribs and the feet in the left iliac fossa, the back anteriorily, and to the right the shadow of the placenta could be seen apparently attached to the left abdominal wall. On section a thin amniotic sac appeared adherent to the transverse colon and small intestines, and it was impossible to pass the hand around the sac. It was opened at the edge of the placenta, the fluid carefully removed and the child delivered. The fetus was 55 cm. long, weighed 7½ pounds and had been dead several weeks. The effort to remove the placenta was followed by such hemorrhage that it could not be continued. The sac was sewed carefully to the peritoneum, and the wound left open and loosely packed with gauze, which was changed daily. Twenty-seven days after the operation about half of the placenta could be removed without giving the patient pain; a few days later the entire placenta was removed. The wound was kept packed with gauze and several ounces of 1 per cent dichloramin-T were poured into the cavity daily until it became sterile. The abdomen healed perfectly without additional suture. The wide open drainage, it is thought, was responsible for the mother's rapid recovery. The incision was made along the border of the right rectus muscle, and this was thought to be favorable for the complete and rapid union. The blood vessels at the placental site did not close until forty-three days after the death of the child.

Cesarean Section at Seven Months for Premature Detachment of the Placenta in Bifid Uterus.—CARAVEN (*Gynéc. et Obst.*, 1924, **9**, 184) reports the case of a woman, aged twenty-two years, who had suffered with pain and distress at menstruation. She was about seven months in her first pregnancy. On examination a bifid uterus was found with a pregnancy developing in the left cornu of the uterus. There were symptoms of irritation and pain, and the patient was put at rest with hot applications. She improved and the tumor in the left side increased in size. It gradually assumed the proportions of a seven-months' uterus. The head of the child was uppermost and the body was flexed from left to right. The patient was taken with considerable hemorrhage and premature separation of the placenta was diagnosed. The placenta was above and to the left near the fetal head. At operation the bifid uterus was present, and the pregnancy was as had been diagnosed. The placenta had partially separated. A section of the uterus was at once made, delivering the child, followed by supravaginal hysterectomy with the removal of the appendages. The mother and child made a good recovery.

Hydatid Moles in the Uterus.—BELL (*Jour. Obst. and Gynec. Brit. Emp.*, 1924, **31**, 276) describes the case of a woman, aged twenty-four years, a multipara, admitted to the hospital with complete amenorrhea, except for a slight show for one day. The uterus was the size of twelve weeks' pregnancy, the cervix soft and the body of the uterus boggy in consistence. Anterior hysterotomy was performed and a mole easily removed. The patient made an uninterrupted recovery.

On examination the specimen was a mass which comprised vesicles mixed with blood clots; there was a small amniotic cavity without an embryo. On microscopical study the villi had undergone degeneration, and there was considerable blood clot. The specimen was that of a blood mole. The patient stated that her last menstruation had begun and ended eleven months before her admission to the hospital for treatment. The mole had been carried in the uterus then for a considerable time. WILSON (*Ibid*) reports the case of a multipara who had ceased to menstruate, morning sickness had developed and the ninth month after the cessation of menstruation the patient came for examination and the uterus was found to be about four weeks' pregnancy in size, cystic, with a soft cervix. There were no distinctive changes in the breasts or vagina. An examination was made a month later, and there had been no increase in the size of the uterus. The uterus was emptied by passing bougies and giving pituitrin followed by the very slow expulsion of a mole. The patient had a chill following this, but the temperature fell to normal and the patient recovered. On examination there was an amniotic cavity containing a fetus 12 mm. in length, while the remainder of the specimen consisted of vesicles which were degenerated villi.

Pregnancy Complicated by Encephalitis Lethargica. HERD (*Jour. Obst. and Gynec. Brit. Emp.*, 1924, **31**, 267) reports the case of a primipara, aged twenty-four years, with headache and edema of the ankles in the thirty-sixth week. After severe frontal headache the patient had what was said to be a convulsion, and was removed to the hospital as a case of eclampsia. On admission she was restless, her color was good, station was normal and blood-pressure was 130. The gestation was normal at the thirty-sixth week. The cervix admitted two fingers and the membranes could be felt. The urine taken by catheter was highly albuminous; within six hours after admission the patient had six fits without cyanosis and regained consciousness within five minutes. Then there were convulsions with marked cyanosis similar to those of eclampsia. Consciousness was gradually regained, and labor developed with spontaneous birth of a living male child. The placenta was delivered spontaneously and showed no abnormality. For the first five days after delivery the patient remained partially comatose, restless, with rhythmic contraction of the muscles of the lower jaw, temperature ranging from 99.6° to 102° F. Albumin was always present in the urine, but the blood urea was not high. Involution proceeded normally. The patient had been treated by lavage of the colon, blood transfusions with citrated blood and two injections of morphin (¼ gr.) were given on the first day. The patient was transferred to a general hospital, where she died on the twentieth day after delivery. At autopsy a careful search was made for evidences of toxemia but none were found; the condition was typically encephalitis lethargica. His second case was a primipara who in the thirty-fifth week became sleepless and neuralgic, attributed to fright. There was nothing to suggest toxemia. On admission to the hospital the patient was excited, restless, rational and with a normal pulse and temperature. There were continuous movements of the muscles of the head, face and limbs. The eyes were normal and so were the reflexes. The urine contained con-

siderable albumin. The thyroid gland was not enlarged, and the patient was very constipated. At first she was thought to have chorea, but treatment addressed to this condition was without result, and the case was then recognized as one of encephalitis lethargica. On the fourth day the patient gave birth to a still-born, non-macerated female child, and during labor and afterward was unconscious for some time. The temperature rose from 100° to 102° F. During the next four days she was semiconscious, restless with delusions and subsequently her condition improved, but complete recovery did not occur and is not expected. Postmortem examination of the child revealed nothing of significance.

A Study of the Syphilitic Placenta.—MÖNCKEBERG and AVILÈS (*Gynéc. et Obst.*, 1924, **9**, 419) have made a histological and pathological study of the syphilitic placenta, and illustrate their findings. The predominant lesion is that of hematosis which, in proportion to its severity, affects the nutrition of the fetus. The different lesions found were infarcts, endarteritis, necrosis of the villi, thrombosis, hemorrhage, the diminution in the capacity of the blood channels of the placenta—these conditions may result in the death of the embryo. The writers bring up the question of the presence of the treponema pallidum in the syphilitic placenta. They could not successfully isolate this germ in the placenta and question whether this was due to faulty technic. In 30 per cent of the fetuses studied in these cases the treponema was found in the liver, so that they believed the failure to find it was not through an error in technic.

The Live Method of Obstetric Teaching.—GREEN and ARMYTAGE (*Jour. Obst. and Gynec. Brit. Emp.*, 1924, **31**, 218) state that the roentgen-ray study of labor made by Warnekros, and Hollands' *Researches on Intracranial Strains* has thrown new light on the mechanism of labor and require new methods of demonstration and teaching. To make teaching more interesting the writers take twenty students at a time for six weeks: each morning one hour is devoted to clinical gynecology and one hour to clinical obstetrics. They use for demonstration an especially made large female dummy, lined with a clean warm turkish towel, and in this is placed, shortly after it has been nursed, a recently born baby, up to ten days old. One by one the different presentations are taken up, the mechanism of labor is demonstrated and complications and treatment reviewed. The movements of the live child, clothed in one thickness of garment only, impress the student. The cord is illustrated by red tape sewed to the clothing, and with the dummy turned on its left side the reason for flexion and the mechanism of the perineum can be observed. By placing one or more small flat hand towels under the lining towel, between the sacral promontory and the baby's head, a moderate contraction of the pelvic brim of the model is made, and the study can be carried out of the relation of the head to the pelvic brim, and the various tests of labor. The writers make every demonstration a clinical lecture, using living material on all occasions. Classes should be held in a warm room near the lying-in ward. Each class should not be greater than twenty. The assistance of nurses is always needed. The baby should be a small and

healthy one, and if carefully handled no harm can be done. In inducing labor when a bougie could not be obtained, the writers have used rubber tubing, into which they inserted a thin piece of bambo or flexible stick; a piece of silk was tied tightly around the tubing just above the end of the stick. To demonstrate the method with the live baby, a conical bag of clean canvas or linen was used which was fitted loosely over the child's head, with the apex representing the cervix. This apex of the bag may be grasped by forceps, opened with scissors to represent the open cervix and bougie can then be introduced as a demonstration. By using rubber sheeting the pelvic floor can be represented and its mechanism and lacerations can be taught. The placenta can be represented by a sponge and other similar methods are available. The writers believe that when inexpensive materials are employed, the constant presence of the instructor and the use of living material will make obstetric teaching far more efficient. He does not believe the use of a still-born fetus is efficient. He adds two illustrations, with small tracings of the pelvic floor.

Etiology of Certain Congenital Defects.—Bagg (*Am. Jour. Obst. and Gynec.*, 1924, **8**, 131) contributes an illustrated paper upon this subject, presented before the New York Obstetrical Society. His work consisted of experiments upon animals to determine the effect of the roentgen-ray and other sources of possible malformation. He finds that structural defects arise from arrested development with blood vascular disturbances. In some cases this is poor blood affecting the vascular endothelium or other conditions in the vessels. The local area of such extravasation occurring at a critical period in the development of an organ may interfere with processes of development and thus lead to structural defects. In experimental work the eyes of animals are often affected because the bloodvessels of the head readily give away and permit extravasation of blood. Club feet and syndactylism are the result of these changes in the extremities. Entire organs are sometimes affected, such as the kidneys, and their development may be partially or wholly suppressed. In newborn children many such lesions in the head can be traced to birth injury by instruments, pelvic pressure or partial asphyxia and increased blood-pressure during labor. Similar hemorrhages, however, have been found in children examined in the uterus during Cesarean section. In these cases birth pressure plays no part. Congenital nevi indicate that such blood disturbances occur in the prenatal period. Club feet are often ascribed to the faulty position of the child in the uterus or to paralysis and malformation of the affected limb. No light is thrown on this subject by the study of the development of abnormal structure. Cases where the eye is poorly developed or is entirely lacking may be traced to these blood vascular disturbances.

Anesthesia in Obstetrics.—Boyle and Hewer (*Jour. Obst. and Gynec. Brit. Emp.*, 1924, **31**, 264) have summarized their experience at St. Bartholomew's Hospital. For analgesia during normal labor the patient is allowed to give herself nitrous oxide as she feels the pains approaching. For the application of forceps pure gas-oxygen they believe to be an ideal method. For Cesarean section, in addition

to gas-oxygen, some ether is necessary, and if the percentage of oxygen be increased just before delivery the baby will be bright red in color and will cry instantly. The suturing of the uterus and of the abdominal wall can generally be done under gas-oxygen alone, as the muscles have been stretched during pregnancy and absolute relaxation is unnecessary. This method of anesthesia also suffices for induction of labor and other vaginal operations. A highly nervous patient may receive morphin and scopolamin before taking the gas-oxygen and ether or ethanesal. As regards spinal anesthesia, they do not consider it safe in comparison with general anesthesia. The mortality of this method they believe to be about 1 in 400. They believe that the endotracheal method of anesthesia will be superior to others for major pelvic surgery. They advocate the combination of gas-oxygen, ethanesal and chloroform. The patient is first anesthetized fairly deeply by inhalation, and under the guidance of a laryngoscope a tracheal catheter is passed and gas-oxygen and chloroform are given down the catheter until the patient ceases to cough, and the chloroform is turned off and ethanesal substituted. Respiration is extremely shallow, and can be stopped if desired and the color of the patient is always good. This results in an absolutely relaxed abdominal wall and without protrusion of the intestines and without congestion of the lungs. This must be given with proper apparatus and by an expert to be successful.

GYNECOLOGY

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Chemical Hysterectomy.—Chemical hysterectomy is presented by BABCOCK (*Amer. Jour. Obst. and Gynec.*, 1924, **7**, 693) as an additional measure for the removal of the essential parts of the uterus, but it is to be used with care and good judgment. It has a somewhat limited field and will not eliminate the use of radium in gynecology or the scalpel for hysterectomy. Obviously more dangerous than radium and, therefore, not even a competitor against the simpler forms of uterine bleeding, it has the advantage of permanency of action and the elimination of any associated uterine infection. It is probably more certain than simple ligation of the Fallopian tubes or the use of the roentgen-ray or radium in producing sterility and some surgeons may welcome this method as a means of escaping from an occasional very difficult or dangerous hysterectomy. In performing this operation the patient is prepared and placed in position as for a uterine dilatation. Local, nitrous oxide or narcotic anesthesia may be used. The cervix and inter-

nal os are dilated sufficiently for the introduction of a uterine packer. The cavity of the uterus is explored and scrapings or discharge is removed for laboratory study. A uterine packer, preferably with an obturator is introduced well through the internal os and the cavity of the cervix and uterus thoroughly packed with a narrow gauze tape impregnated with a saturated solution of chlorid of zinc. During this procedure the vagina is protected with a strip of gauze impregnated with dry sodium bicarbonate that extends from behind the cervix out under the weighted vaginal speculum. The vagina is now so packed with other strips of soda-impregnated gauze that the cervix and the caustic tape issuing from the cervix, are completely surrounded. The packing, including the caustic tape, is withdrawn in seventy-two hours or less, dependent on the amount of gauze used and the thickness of the uterine walls. The uterine slough will usually come away about the end of a week and it is wise to keep the patient in bed one week and under supervision for nine days. Rarely is a secondary packing required. Marked secondary oozing is not usual, but should it occur, the patient should be put in the knee-chest position, a speculum inserted and the vagina carefully packed with gauze after dusting in 5 or 10 gr. of alum. If the slough has not been expelled by the ninth day, it should be removed by forceps or the finger, provided it is no longer attached to the uterine wall. Babcock gives specific instructions concerning the preparation of both the caustic tape and the alkaline gauze and also the method of computing the length of time that the tape should be left in place in various types of cases.

Etiology of Cancer.—For many years WILLY MEYER (*Jour. Cancer Research* 1924, **8**, 45) has been deeply interested in the subject of cancer and its causation and in his Presidential address before the American Association for Cancer Research he summed up his present belief concerning the etiological factors in cancer. He reminds us that by general agreement of competent investigators the observation is throughout accepted as a fact that spontaneous cancer cells descend from normal cells of the tissue in which the cancer arises. To the process of transformation of the cells from one state to the other, parasites, like numerous other non-specific factors, such as mechanical, thermal, actinic, chemical, endocrine, hereditary, stand in the relation of the match to the heat radiating from the fire which it has kindled, viz. inciting but incidental. Current experimental production of primary cancer by various non-specific means makes the search for the specific cancer agent appear as no longer advised, and seems to prove that irritation is ordinarily the starting point of developments tending in the direction of cancer. As nearly as anything can be certain in medicine, there is no cancer contagion or specific infection, since observations seem to prove that cancer is in every instance an individual experience. More than one individual may receive a non-specific inciting factor from the same source, and then independently, by reason of the same, may or may not develop cancer. Around a source disseminating directly, or indirectly through intermediate hosts, one or more non-specific inciting factors, "cancer houses," "cancer districts," "cancer towns" may grow up and in order to reduce cancer incidence such common sources should be sought out and abated. One such source seems

to be the rat. Systematic rat extermination, already suggested for economic and hygienic reasons, appears advisable from the point of view of reducing the number of cancer-inciting factors. From the same point of view prophylactic anthelmintic treatment at frequent regular intervals throughout life, applied as broadly as vaccination against smallpox, might possibly work a reduction of cancer incidence, according to Meyer. Such a proceeding would be of still greater value if in addition means could be found to reach and render harmless the larvæ in the various organs.

The Time for Operation in Ectopic Gestation.—There always has been and probably always will be a controversy as to whether ruptured ectopic pregnancy demands an immediate operation or should be watched temporarily until the period of shock is passed. All will agree that it is most dangerous to operate while the patient is in shock, but on the other hand, in some cases of the tragic type, the patients never react and die if untreated. Some interesting studies on the systolic blood-pressures in these cases have been made by WELTON (*Amer. Jour. Obst. and Gyn.*, 1924, **7**, 158) who concludes that nothing is gained by operating while a patient is in shock for he states that if the patient does not die at the time of her initial collapse, it denotes she will respond, to a certain degree, to measures in treatment. He believes that all ectopic pregnancy cases should be given a trial to demonstrate what they can do by way of a recovery, which will be well shown by the systolic blood-pressure readings. In all unruptured ectopics, surgery is the rule. If the pressure continues to fall in spite of treatment, surgery is imperative. Similarly, in a pressure that reacts to, at the maximum, 115 mm., operation is indicated, because if the pressure is permitted to return to normal, the sealing clot may be disturbed and renewed hemorrhage and shock occur. In the moribund type of case, with an initial pressure of 50 or lower, the rise is never back to normal limits. It is important to remember that a pressure that rises and then remains stationary calls for surgery: The length of time to wait while a pressure remains stationary depends upon the type of case, and is governed by the experience of the operator. Any pressure that rises and then begins to fall calls for immediate surgery. On the whole, the systolic blood-pressure is a very good index of the patient's condition.

PATHOLOGY AND BACTERIOLOGY

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A Study of Hypersensitiveness to Derivatives of Hemolytic and Non-hemolytic Streptococci.—MACKENZIE and HANGER (*Proc. Soc.*

Exper. Biol. and Med., 1924, **21**, 442) tested a large number of patients with a variety of conditions, using filtrates and extracts of hemolytic and non-hemolytic streptococci obtained from the interior of tonsils immediately after tonsillectomy. The intracutaneous injection of 0.01 to 0.04 cc of filtrates of young broth cultures produced in nearly all adults positive reactions, which developed after a latent period of eight to twelve hours. The intensity of the reaction varied from a central red, slightly tender elevation surrounded by slight swelling and erythema, 1.5 to 2.5 cm. in diameter, to stronger reactions consisting of a central pustule which always proved to be sterile on culture. The pustule was surrounded by a red, hot, indurated zone with an erythematous halo, measuring as much as 10 to 12 cm. in diameter. The full intensity of the reaction was attained after twenty-four to forty-eight hours, fading in two to ten days and leaving a pigmented spot with a fine desquamation in some cases. Very young children did not react to the substance. The non-hemolytic streptococci obtained from routine throat cultures in the absence of acute infection were much less capable of producing active filtrates than non-hemolytic streptococci obtained from excised tonsils. Certain non-hemolytic streptococci quickly lost the capacity to produce the active substance when cultivated outside the body. The active substance present in the twenty-four-hour filtrates withstood boiling and did not rapidly deteriorate when kept at ice-box temperature. Some individuals reacted more strongly to filtrates, others to constituents of the bacterial cell.

Lesions of the Aorta Associated with Acute Rheumatic Fever and with Chronic Cardiac Disease of Rheumatic Origin.—"The question as to whether the still unknown virus of acute rheumatic fever may localize in the aorta has not been satisfactorily answered." Consequently, PAPPENHEIMER and VON GLAHN (*Jour. Med. Research*, 1924, **44**, 489) conducted a comparative histological study of the aortæ in a series of 76 rheumatic cases, and in 77 non-rheumatic cases, dying from a variety of diseases, as well as an equally large series of syphilitic aortitis cases. In the selection of cases for the rheumatic group the authors based the diagnosis upon the clinical history of one or repeated attacks of rheumatic fever, or of chorea, or of repeated attacks of tonsillitis; upon the finding of typical rheumatic lesions at autopsy, namely, verrucose endocarditis, showing the characteristic structure and absence of bacteria in sections; upon Aschoff bodies in the myocardium associated in the recurrent cases with the elliptical perivascular areas of fibrosis; upon fibrinous pericarditis or pericardial adhesions, and chronic mitral disease, not arteriosclerotic. The sections for microscopical examination were stained with hematoxylin-eosin, with Weigert's elastic tissue stain, followed by hematoxylin and van Giesen's picrofuchsin and with the Una-Pappenheim methyl-green-pyronin method. The most distinctive lesions encountered in the rheumatic group were the dense and often acellular scars in the vicinity of the nutrient vessels, and the Aschoff cells or nodules in the adventitia. In comparing the lesions with those found in syphilis, the authors called attention to the fact that in syphilis there is a much greater lymphoid and plasma cell reaction in both media and adventitia. The rheumatic scars

remained confined to the vicinity of normal penetrating vessels, whereas the syphilitic granulation tissue was attended by the formation of new capillaries and the resultant scars were far more extensive and led to a far greater destruction of elastic and muscular fibers. The authors concluded that "further study is necessary to determine the distribution of the lesions in the aorta, the possible occurrence of similar changes in peripheral vessels and their clinical significance."

Inoculation and Implantation Experiments in Monkeys with Glands from Cases of Hodgkin's Disease.—The experimental results obtained in Hodgkin's disease can be placed in one or other of the three following categories: (1) The production of a tuberculous lesion in experimental animals by the injection of Hodgkin gland emulsions (Cignozzi, 1906; Schaeffer, 1914); (2) the reproduction of the histological changes of the disease as seen in man by the injection of cultures of a diphtheroid bacillus recovered from the lymph glands in cases of Hodgkin's disease (Bunting and Yates, 1913, 1914); (3) negative findings (Longcope, 1908; Torrey, 1916; Cunningham and McAlpin, 1923). These various results are in keeping with the different views as to the etiology of Hodgkin's disease, arrived at by various observers on other grounds, namely, that it is: (1) An atypical form of tuberculosis; (2) a specific infection by a diphtheroid bacillus; (3) a granuloma of unknown etiology; (4) a neoplastic disease. STEWART and DOBSON (*Brit. Jour. Exper. Path.*, 1924, **5**, 65) inoculated 3 rhesus monkeys with lymph glands from a case which showed a well-marked eosinophilia in the glands and 1 bonnet monkey with the glandular material from a case which did not show eosinophile cells, but which exhibited microscopically, typical, active cellular Hodgkin's disease. In each experiment laparotomy was performed, and some small chips of a Hodgkin gland just excised from the patient were implanted into some of the mesenteric lymph glands or into the spleen, or both. One rhesus monkey, after four and a half months, showed an unusual degree of simple hyperplasia of the lymphoid follicles and of the Malpighian bodies of the spleen, especially of the germ centers in each instance, together with a peculiar giant-cell reaction, probably of foreign-body type, around the implanted material. The remaining experiments yielded completely negative results, the bonnet monkey being under observation for three years and 1 Macacus rhesus for two years before they were sacrificed for examination. The authors conclude by saying that "These experiments afford further proof that whether or not Hodgkin's disease is an infective granuloma, it is at least not due to a virus capable of reproducing the disease in monkeys."

The Prevention and Cure of Rickets by Means of Bile.—Since it has become well established that cod-liver oil prevents and cures rickets, KAPSINOW and JACKSON (*Proc. Soc. Exper. Biol. and Med.*, 1924, **21**, 472) conducted a series of experiments on thirty-two-day-old rats to ascertain whether products of mammalian liver, in particular bile, might not exert a similar action. The rats were divided into

two groups. To one group freshly obtained gall-bladder bile from the pig was added to a rickets-producing diet which was given for a period of thirty-five days. In the other group rickets was produced by giving the diet and then bile was added to the diet and given to the animals for a period of fifteen days. It was found that 7 cc of pig bile per day prevented the development of rickets in the rats of the first group, while 3 cc of pig bile per day did not completely prevent the development of rickets and 1 cc exerted a well-marked inhibitory action. In the second group 7 cc of pig bile per day completely cured rickets when fed for a period of fifteen days; 5 cc and 2.5 cc of bile per day did not completely cure rickets, although 5 cc exerted a manifestly greater curative action than 2.5 cc. The control rats all showed rickets.

A Fatal Infection with an Organism of the Proteus Group.—As cases of fatal infection with organisms of the proteus group are rare, WARREN and LAMB (*Jour. Med. Research*, 1924, **44**, 375) report an instance which occurred in a man, aged thirty-one years, who was suffering from myelogenous leukemia, tuberculosis and a severe Vincent's angina. The proteus-like organism was isolated from two antemortem blood cultures and from postmortem cultures of the heart's blood, pericardial sac, liver and spleen. According to morphology, mobility, proteolytic activity and fermentation reactions, the organism could be identified as a member of the proteus group, although it did not correspond to any previously described organism. It was pathogenic for laboratory animals, causing septicemia and necrosis of liver, heart muscle and adrenals. The filtrate of young broth cultures were toxic and had similar pathological effects on the tissues to those produced by the organisms.

Variations in the Number of Blood Plates Associated with a Common Cold.—It has been shown that the disappearance of microörganisms from the blood stream into which they have been introduced is preceded by their agglutination and that this agglutination is brought about by the blood plates. From these and other findings it appears that the blood plates are concerned in the resistance to bacterial infection and a determination of plates to the site of action would infer at least a temporary fall in their number in the circulating blood whence they are drawn. BANNERMAN (*Brit. Jour. Exper. Path.*, 1924, **5**, 16) had an opportunity to observe the fluctuation in the daily blood-plate counts of an individual with an apparently arrested pulmonary tuberculosis, who developed an acute nasopharyngeal "cold." The average plate count of this person in his normal condition lay in the region of 340,000 per c.mm. During the "cold" the number fell to about 240,000 per c.mm. until the terminal stages of the "cold," when a rise above the normal average occurred and was then followed by a resumption of the normal level.

HYGIENE AND PUBLIC HEALTH

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Malta Fever: Cattle Suggested as a Possible Source of Infection.—Evans (*Pub. Health Rep.*, 1924, **39**, 501) summarizes her work as follows: Five hundred human serums from patients suffering with a variety of diseases were tested for agglutinins specific to B. melitensis. Fifty-nine, or 11.8 per cent, gave a definitely positive reaction in dilutions of 1 to 5 or higher. One serum had a titer of 1 to 320, which would lead to an unquestioned diagnosis of Malta fever in regions where the disease is endemic. The patient was unaware of any possibility of having contracted an infection from goats. He was in the habit of drinking raw cow's milk. Absorption tests with the serum showed that this patient was infected with the *abortus* (bovine) variety of B. melitensis. The titers of the remaining 58 serums which gave positive reactions varied from 1 to 5 to 1 to 40. The suggested explanation for these positive reactions is that the agglutinins were produced as a specific response to B. melitensis ingested in cow's milk, although such an infection may not necessarily have caused a notable illness.

The Prevalence and Trend of Drug Addiction in the United States and Factors Influencing It.—Kolb and Dumez (*Pub. Health Rep.*, 1924, **39**, 1179) give the following summary and conclusions: The evidence seems to show that a maximum estimate for the number of addicts in the United States at the present time would be 150,000. The estimates based on actual counts and on the available supplies of narcotics, together with the conditions reported by the physicians interviewed, point to about 110,000, which number is believed to be nearly correct. The number of addicts has decreased steadily since 1900. Before this decrease set in there may have been 264,000 addicts in this country. The greater number of addicts in prison at present as compared with former years is due to the rigid enforcement of recently enacted laws and not to an increase in the prevalence of addiction. The average daily addiction dose of the opiates in terms of morphin sulphate or heroin hydrochloride is not less than 6 gr. The dose of cocain hydrochloride is practically the same. The quantities of narcotics imported by this country at the present time are believed to be only slightly in excess of the amounts required to supply medicinal needs. While physicians have been credited with being responsible for the creation of many addicts in the past, it is concluded as a result

of our studies and observations that but few cases of recent addiction can be so attributed. Before the enactment of restrictive laws in this country there was much opium smoking and addiction to gum opium and laudanum. Today addicts use the alkaloids or their derivatives almost exclusively. Cocain hydrochloride was used alone by a large number of addicts prior to 1915, but is now used only in conjunction with the opiates except in a few cases. The proportion of the delinquent type of addict is gradually increasing. This is apparently not due to an increase in the number of this type, but to a gradual elimination of normal types. From the trend which narcotic addiction in this country has taken in recent years as a result of the attention given the problem by the medical profession and law-enforcement officers, it is believed that we may confidently look forward to the time, not many years distant, when the few remaining addicts will be persons taking opium because of an incurable disease and addicts of the psychopathic delinquent type, who spend a good part of their lives in prisons.

Epidemiological Principles Affecting the Distribution of Malaria in Southern United States.—MAXCY (*Pub. Health Rep.*, 1924, **39**, 1113) enumerates the following factors which determine the distribution of malaria: (1) Anopheline mosquitoes which feed upon man must be propagating in sufficient numbers within flight range (about 1 mile) of human habitation; (2) human beings with the sexual forms (gametocytes) of the malaria parasite in their peripheral blood must be accessible to and bitten by these mosquitoes; (3) temperature must favor completion of the life cycle of the parasite in the mosquito; (4) if the level of prevalence is to be maintained, infectible human beings must be accessible to and bitten by infected mosquitoes so that at least one new infection occurs for each old one that recovers. Given the conditions which we at present know to be favorable, a careful survey for enlarged spleens or parasites may (or may not) show a malaria problem to be present. On the other hand there are large areas where conditions exist which are obviously unfavorable to the transmission of malaria, that is where the population is composed of enlightened, well-to-do white families living in well-screened houses in prosperous sections on cleared, cultivated, and thoroughly drained farm land and in towns with the best sort of medical attention. To persons living under these conditions malaria is practically an unknown disease. It follows, then, that malaria is not an ubiquitous disease in southern United States, as is, for instance, such a disease as measles. It exists where certain more or less well-known requirements as to the mosquito host and the human host are realized. *Malaria is characteristically a focally distributed disease.*

Foci are classified as follows: (1) Endemic—where conditions are favorable for the transmission of malaria year after year. (2) Epidemic—universal prevalence, usually due to new conditions or circumstances. It should be emphasized that there may be a considerable element of chance in epidemic outbreaks of this type. It is a fortuitous circumstance that at the particular time when Anopheles are more abundant than usual, a malaria patient with many gametocytes in the peripheral circulation is housed in a location most exposed to the bites of these mosquitoes; and that subsequently, although perhaps only one

of these mosquitoes survives to become infective, this mosquito happens to reach a room or a tent in which many persons are sleeping and takes an infecting blood meal on several of them, thus precipitating an outbreak. There are many places in this chain of events where the sequence may be and probably is interrupted much more frequently than it is successfully completed. (3) Potential—where one or another form is usually absent but where all may occasionally be present, resulting in an outbreak. For instance, all the factors may be present at a given time except a carrier accessible to the bites of Anopheles; and, if one happens along at this particular time, transmission occurs. Or, all the factors may be present except a sufficient number of Anopheles, the creation of a small pool of water by the filling up of an old drainage ditch or culvert, or by the building of a roadway, having furnished the missing link. In a prison outbreak, the production of a small number of A. quadrimaculatus in close proximity to a crowded, unscreened camp, constituted a potential focus. It became an epidemic focus when a human carrier appeared upon the scene.

Maxcy's summary is as follows: The factors favorable for the transmission of malaria in southern United States are now fairly well known. The disease is not ubiquitous, but exists in those localities where certain rather highly specialized conditions are realized. Where these conditions are present continuously year after year, the focus is endemic, where brought into existence suddenly by some unusual circumstances, the focus is epidemic; where they may be realized at any time, though one or another factor is usually absent, the focus is potential. Numerical expression of the amount of malaria in a given rural area is not so necessary to the practical health administrator as is a clear understanding of the distribution of the disease. Sufficient field study should be made to establish the localities in which the disease is indigenous and the relative importance of different foci to the surrounding country from an epidemiological point of view. Efforts to control the disease must be directed ultimately toward the endemic centers. The measure of effective control is the demonstration that the amount of malaria transmission taking place is no longer considerable so far as community measures are concerned.

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